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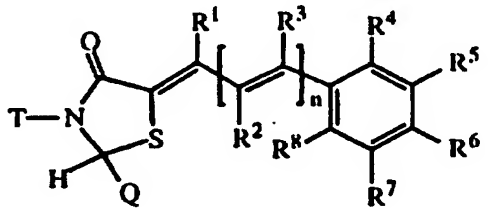
(57) Abstract

The present invention relates to novel thiazolidin-4-one derivatives having formula (I), which inhibit platelet-activating factor and/or 5-lipoxygenase for the prevention or treatment of inflammatory and allergic disorders mediated by platelet-activating factor and/or leukotrienes, and to pharmaceutical compositions containing these compounds, and to the use thereof to inhibit PAF and/or leukotriene. A process for preparing these compounds is also included in the present invention, wherein n, T, Q, R^1, R^2, R^3, R^4, R^5, R^6, R^7 and R^8 are respectively as defined in the description.



(I)

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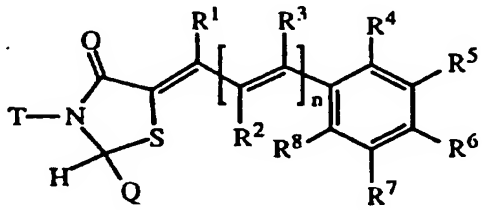
NOVEL THIAZOLIDIN-4-ONE DERIVATIVES

BACKGROUND OF THE INVENTION

Field of the Invention

The present invention relates to novel thiazolidin-4-one derivatives having the following formula(I), which inhibit platelet-activating factor and/or 5-lipoxygenase for the prevention or treatment of inflammatory and allergic disorders mediated by platelet-activating factor and/or leukotrienes, and to pharmaceutical compositions containing these compounds, and to the use thereof to inhibit PAF and/or leukotriene.

A process for preparing these compounds is also included in the present invention.



(I)

wherein, n, T, Q, R^1, R^2, R^3, R^4, R^5, R^6, R^7 and R^8 are respectively defined as the below.

Description of the Related Art

Benveniste et al. found a factor in 1972 which strongly induces platelet aggregation from rabbit basophils. This factor was named platelet-activating factor (hereinafter referred to PAF). Hanahan et al. indentified the factor in 1980 as a phosphoglyceride of the alkyl ether type having an acetyl group in the 2-position, i. e. 1-*O*-hexadecyl or octadecyl-2-acetyl-*sn*-glyceryl-3-phosphocholine.

The physiological roles of PAF have been intensively investigated, and it is known that PAF is an important factor acting on platelet aggregation, reduction in blood pressure, immediate allergic reaction, contraction of smooth muscle, inflammation, pain, edema, and alternation in the respiratory and circulatory systems. Therefore, PAF-antagonistic activity-possessing compounds are very useful for

treating various PAF-induced diseases, such as inflammatory diseases, allergic diseases, anaphylatic shocks, septic shocks, vascular diseases as DIC, myocardinal diseases, asthma, pulmonary edema, and adult respiratory diseases.

Leukotrienes, like PAF, are potent lipid mediators of a variety of topical and systemic diseases and disorders. A 5-lipoxygenase in cytoplasm catalyzes the conversion of arachidonic acid to leukotriene A4 which is the precursor of leukotriene B4 and C4. Leukotriene B4 and C4 are oxygenated metabolites that contribute to the pathogenosis of such inflammatory disorders as arthritis, asthma, psoriasis, and thrombotic disease. Leukotrienes are released concomitantly from leukocytes with PAF from a common phospholipid precursor upon cellular activation and act synergistically with PAF in many biological models.

It has been demonstrated by O'Donnell and Lewis et al. that a physical combination of a PAF antagonist and leukotriene inhibitor is significantly more effective than either agent alone in treating athma in an animal model [Therapeutic Approaches to inflammatory Diseases, Lewis et al., Elsevier, New York, 1989, pp 169~193]. Shen et al. and Page et al. pointed out that single compounds which possess the dual inhibitory activity of PAF and leukotriene inhibition would have greater anti-inflammatory activities than a physical combination of a PAF and a leukotriene inhibitor. [PAF and Related Lipid Mediators, Plenum Pub., N.Y., 164 (1987) ; Trends in Pharmacol. Sci., 10(1989)].

Moreover, the chemical combination of PAF and 5-lipoxygenase inhibitory activities in one molicule has advantages over drug combinations in terms of optical pharmacokinetics, clinical applications and developmental costs.

Under these circumstances, various thiazolidin-4-one derivatives have been synthesized. But thiazolidin-4-one compounds simutaniously possessing PAF-antagonistic activity and leukotriene inhibition activity have not been known at this time.

Reports related to thiazolidin-4-one derivatives are as followings: *N*-(phenyl,

pyridyl)-2-pyridyl-thiazolidin-4-one derivatives for agricultural chemicals [Japanese Patent Kokai No. 145679/79]; *N*-(phenyl, benzyl, cycloalkyl)-2-pyridyl-thiazolidin-4-one derivatives for agricultural chemicals [Japanese Patent Kokai No. 55184/80]; *N*-(carboxycyclohexylmethyl)-2-pyridyl-thiazolidin-4-one derivatives for anticomplementary acitvity [Japanese Patent Application Kokai No. 85380/82]; *N*-(carboxymethylphenyl)-2-pyridyl-thiazolidin-4-one derivatives having anti-inflammatory and analgesic activity [Japanese Patent Kokai No. 88170/82]; *N*-(pyrazinyl)-2-pyridyl-thiazolidin-4-one derivatives for agricultural chemicals [Japanese Patent Kokai No. 183689/83]; *N*-(phenyl)-2-pyridyl-thiazolidin-4-one derivatives for intermediates in synthesis [U.S. Patent No. 4,501,746]; *N*-(carbamoyloxy)-2-pyridyl-thiazolidin-4-one derivatives for cardiotonic[Japanese Patent Kokai No. 103883/86]; *N*-(alkyl, aminoalkyl)-2-pyridyl-thiazolidin-4-one derivatives for PAF-antagonist [Japanese Patent Kokai No. 126391/87, 139304/87, 160481/87, 12379/88 and European Patent Application No. 292305/88] etc..

Because of the large number of diseases and disorders which are mediated by PAF and leukotrienes, synthesis of new compounds which possess leukotriene or PAF inhibitory activity, and preferably compounds which possess both inhibitory activity will be very useful as active ingredients in the prevention and/or treatement of those diseases and disorders.

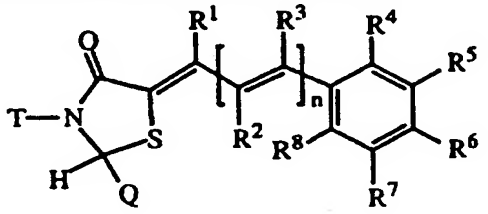
Accordingly, the present inventors have conducted long term investigations and studies on thiazolidin-4-one derivatives which have PAF antagonistic acitvity and/or leukotrienes inhibitory activity. The present invention has been accomplished based on these findings.

SUMMARY OF THE INVENTION

It is an object of this invention to provide novel thiazolidin-4-one derivatives which act as PAF antagonists and/or inhibit biosynthesis of leukotrienes via the 5-lipoxygenase pathway, the pharmaceutical uses of these derivatives, and a process for

preparing them.

The present invention relates to the novel thiazolidin-4-one derivatives having the following formula(I), which act as PAF antagonists and/or inhibit biosynthesis of leukotrienes via the 5-lipoxygenase pathway.



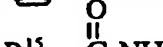
(I)

wherein, :

n is 0, 1, 2 or 3;

Q is C_1 ~ C_{10} alkyl group, phenyl group that is optionally substituted with one or more suitable substituents selected from methoxy group and nitro group, or pyridiyl group that is optionally substituted with one or more methyl group;

R^1, R^2 and R^3 are independently hydrogen atom, C_1 ~ C_{10} alkyl group, C_3 ~ C_6 cycloalkyl group, or phenyl group that is optionally substituted with one or more methoxy group;

R^4, R^5, R^6, R^7 and R^8 are independently hydrogen atom, hydroxyl group, halogen atom, C_1 ~ C_{10} alkyl group, C_1 ~ C_{10} alkoxy group, nitro group, amino group that is optionally substituted with one or more suitable substituents selected from C_1 ~ C_{10} alkyl group and C_3 ~ C_6 cycloalkyl group, phenyl group that is optionally substituted with one or more suitable substituents selected from methoxy group and nitro group, C_1 ~ C_{10} haloalkyl group,  , $-CO_2H$, $OCH_2OCH_2CH_2OCH_3$, $-OCR^{15}$, $-OCOR^{15}$, $-CR^{15}$, $-CNHR^{15}$, $-COR^{15}$, $-NHCR^{15}$, $-CH_2NHR^{15}$, $-N(OH)CNHR^{15}$, $-CN(OH)R^{15}$, $-NHCN(OH)R^{15}$, $-CH_2NHCN(OH)R^{15}$, $-OCNR^{15}R^{15}$, $-OC(R^{16})_2COR^{15}$, $-OCH_2OCR^{15}$, $OCCH_2)_mCOH$, or $-OCCH_2)_mCOR^{15}$ (in which R^{15} is C_1 ~ C_{10} alkyl group; m is 1, 2, 3 or 4); and

T is hydrogen atom, hydroxyl group, $C_1 \sim C_{10}$ alkyl group,

$-(CH_2)_m-R^9$, $-(CH_2)_m-O-R^{10}$, $-(CH_2)_m-\overset{O}{\overset{\|}{C}}-R^{11}$, $-(CH_2)_m-NH\overset{O}{\overset{\|}{C}}-R^{12}$,

$-(CH_2)_m-N(OH)\overset{O}{\overset{\|}{C}}-R^{16}$ $-(CH_2)_m-N(OH)\overset{O}{\overset{\|}{C}}NH_2$, $-(CH_2)_m-\overset{O}{\overset{\|}{C}}N(OH)-R^{16}$,

or $-(CH_2)_m-NR^{13}R^{14}$ (in which, m is 1, 2, 3 or 4; R^9 is hydrogen atom, phenyl group that is optionally substituted with one or more suitable substituents selected from $C_1 \sim C_6$ alkyl group and $C_1 \sim C_6$ alkoxy group, or a pyridyl group; R^{10} is hydrogen atom, $C_1 \sim C_{10}$ alkyl group, or $C_1 \sim C_4$ alkanoyl group; R^{11} is $C_1 \sim C_{10}$ alkyl group, $C_1 \sim C_{10}$ alkoxy group, or amino group that is optionally substituted with one or more suitable substituents selected from $C_1 \sim C_{10}$ alkyl group and $C_3 \sim C_6$ cycloalkyl group; R^{12} is $C_1 \sim C_{10}$ alkyl group or phenyl group; R^{13} is hydrogen atom, $C_1 \sim C_{10}$ alkyl group, or $C_1 \sim C_{10}$ alkanoyl group; R^{14} is hydrogen atom or $C_1 \sim C_{10}$ alkyl group or when taken together, connecting R^{13} and R^{14}, a substituted or unsubstituted four- to seven-membered cycloamino group, or a cycloamino group having another hetero atoms; and R^{16} is hydrogen atom or $C_1 \sim C_{10}$ alkyl group.

The present invention also includes pharmaceutically acceptable salts of the formula(I), including, for example, salts with mineral acids such as, e.g., hydrochloric acid, hydrobromic acid, phosphoric acid or sulfuric acid, or salts with organic carboxylic acid such as, e.g., formic acid, acetic acid, malic acid, citric acid, maleinic acid, fumalic acid or tartaric acid.

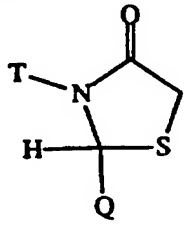
And the compounds according to the invention, as well as the pharmacuetically acceptable salts thereof, may be existed geometrical or optical isomerism. Thus the present invention includes isomer in each case the isomerism and hydrate of the compounds.

DETAILED DESCRIPTION OF THE INVENTION

It is to be understood that both the foregoing general description and the following detailed description are examplary and explanatory, and are intended to

provide further explanation of the invention as claimed.

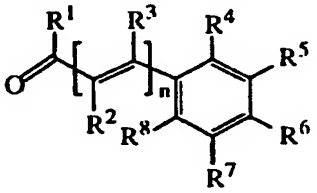
Novel compounds(I) of the present invention can be prepared by reacting compound of formula(II)



(II)

wherein, T and Q are defined as in the formula(I);

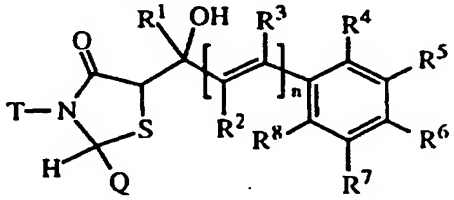
with compound of formula(III)



(III)

wherein, n, R^1, R^2, R^3, R^4, R^5, R^6, R^7 and R^8 are defined as in the formual(I);

in the presence of base and solvent at -78 ℃ to reflux temperature, via the formula (I-1) as an intermidate



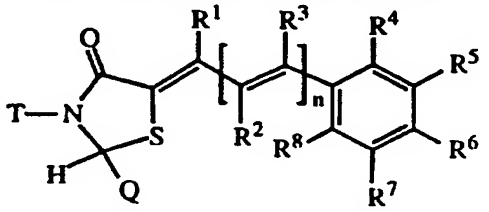
(I-1)

wherein, n, T, Q, R^1, R^2, R^3, R^4, R^5, R^6, R^7 and R^8 are defined as in formula(I).

The reaction of compound(II) with compound(III) is preferably carried out in a suitable solvent which at least one selected from inert organic solvents such as, e.g., tetrahydrofuran, benzene, toluene, dichloromethane or dichloroethane, and polar organic solvents such as, e.g., methanol, ethanol, dimethylsulfoxide, *N,N*-dimethylformamide or acetic acid. The basic medium for the reaction of compound (II) and (III) is preferably metal hydride such as, e.g., sodium hydride, potassium hydride or calcium hydride, lithium diisopropylamide, methyl lithium, butyl lithium, phenyl lithium, sodium methoxide, sodium ethoxide, sodium acetate, sodium

hydroxide, potassium hydroxide, or organic base such as, e.g., triethyl amine, piperidine or morpholine, etc..

Without isolation of the compound of formula(I-1) which is as an intermediate of the reaction mixtures, the reaction mixture can be reacted with an acid or alkali to immediately obtain compound of the formula(I).



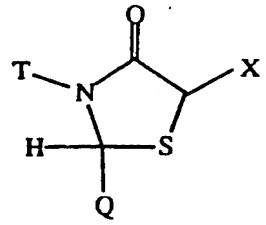
(I)

wherein, n, T, Q, R^1, R^2, R^3, R^4, R^5, R^6, R^7 and R^8 are defined as the above.

Suitable preferred acids are inorganic acid such as, e.g., hydrochloric acid, hydrochloric acid/methanol or hydrochloric acid/ethanol, or organic acid such as, e.g., acetic acid or *p*-toluenesulfonic acid, etc.. And suitable preferred alkalis are sodium hydroxide, potassium hydroxide, sodium methoxide or sodium ethoxide, etc..

If the reaction of compound(II) with compound(III) is carried out at -78 ℃ to 0 ℃, the formula(I-1) as intermidate may be isolated from the reaction mixture in a high yield.

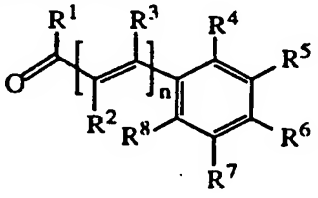
Also, according to the present invention the compound of formula(I) can be prepared by reacting compound of formula(II-1)



(II-1)

wherein, T and Q are defined as in the formula(I), and X is halogen atom;

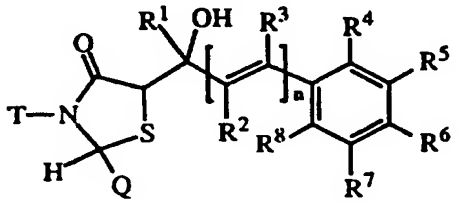
with compound of formula(III)



(III)

wherein, n, R^1, R^2, R^3, R^4, R^5, R^6, R^7 and R^8 are defined as in the formula(I);

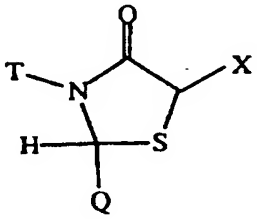
in the presence of zinc and an organic solvent in which tetrahydrofuran, benzene, toluene or trimethoxyborane at -78 ℃ to reflux temperature, to obtain the formula (I-1) as intermidate



(I-1)

wherein, n, T, Q, R^1, R^2, R^3, R^4, R^5, R^6, R^7 and R^8 are defined as in the formula(I); and reacting the compound of formula(I-1) with the said acid or alkali.

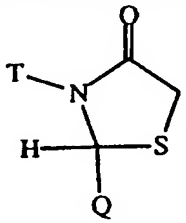
Also, the present invention relates to process for preparing compound of formula(II-1)



(II-1)

wherein, T and Q are as defined in formula(I), and X is halogen atom;

reacting compound of formula(II)

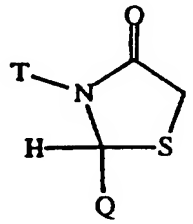


(II)

wherein, T and Q are defined as in formula(I);

with halide such as, e.g., bromine, iodine, chlorine, *N*-bromosuccinimide, *N*-bromophthalimide, *N*-chlorosuccinimide or *N*-chlorophthalimide in an organic solvents such as, e.g., ether, tetrahydrofuran, chloroform, carbon tetrachloride, dichloromethane, benzene, toluene, dimethyl formamide or etc. at 0 ℃ to reflux temperature.

Also, the present invention relates to process for preparing compound of formula(II)



(II)

wherein, T and Q are defined as in formula(I);

by dehydrating the compound of Q-CHO(wherein, Q is defined as in the formula(I)) with compound of T-NH_2(wherein, T is defined in the formula(I)) and mercaptoacetic acid($HSCH_2CO_2H$) in an organic solvent such as, e.g., benzene, toluene, xylene and etc..

It is to be understood that application of the teaching of the present invention to a specific problem or environment will be within the capabilities of one having ordinary skill in the art in light of the teachings contained herein. Examples of the products of the present invention and a representative process for their preparation and recovery appear in the following examples.

EXAMPLE 1.

Preparation of 3-(2-dimethylaminoethyl)-2-(3-pyridyl)-thiazolidin-4-one

< Method A >

A solution of 3-pyridinecarboxaldehyde(1.0 g, 9.15 mmol) and *N,N*-dimethylethylenediamine(0.822 g, 9.15 mmol) in toluene(30mL) was dehydrated under reflux for 1 h. The reaction mixture was allowed to cool to room temperature and evaporated to give 1.63 g(100 %) of *N*-nicotinylidene-*N'*,*N'*-dimethylethylenediamine.

^{1}H NMR(300 MHz, $CDCl_3$) δ : 8.86(d, J=2.4Hz, 1H), 8.64(dd, J=4.8Hz, $\Delta\nu$ = 15Hz), 8.35(s, 1H), 8.11(m, 1H), 7.33(m, 1H), 3.78 (td, J=6.9, 1.2Hz, 2H), 2.68(t, J=6.9Hz, 2H), 2.34 (s, 6H).

To a stirred solution of *N*-nicotinylidene-*N'*,*N'*-dimethylethylenediamine(1.63 g) in toluene(30mL) was added mercaptoacetic acid(0.64 mL, 9.15 mmol) and dehydrated at reflux for 1 h. The reaction mixture was allowed to cool to room temperature and evaporated to dryness. The residue was purified by flash column chromatography on silica gel to give 2.14 g (93 %) of 3-(2-dimethylaminoethyl)-2-(3-pyridyl)-thiazolidin-4-one.

^{1}H NMR(300 MHz, $CDCl_3$) δ : 8.63(m, 1H), 8.56(d, *J*=2.1Hz, 1H), 7.68(m, 1H), 7.36(m, 1H), 5.93(s, 1H), 3.85~3.77(m, 3H), 2.74~2.69(m, 1H), 2.48~2.44(m, 1H), 2.29~2.21(m, 1H), 2.15(s, 6H).

< Method B >

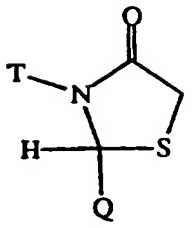
A solution of 3-pyridinecarboxaldehyde(1.0 g, 9.15 mmol) and *N,N*-dimethylethylenediamine(0.822 g, 9.15 mmol) in toluene(3o mL) was dehydrated under reflux for 1 h. To reaction mixture was added mercaptoacetic acid(0.64 mL, 9.15 mmol) and dehydrated under reflux for 1 h. The reaction mixture was allowed to cool to room temperature and evaporated to dryness. The residue was purified by flash column chromatography on silica gel to give 2.24 g(98 %)of 3-(2-dimethylaminoethyl)-2-(3-pyridyl)-thiazolidin-4-one.

< Method C >

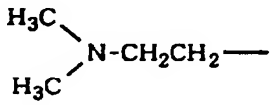
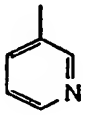
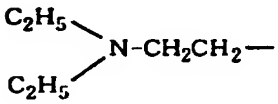
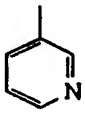
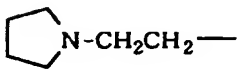
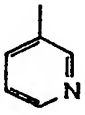
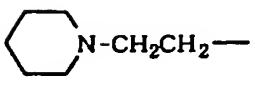
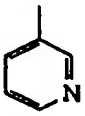
A solution of 3-pyridinecarboxaldehyde(1.0 g, 9.15 mmol), *N,N*-dimethylethylenediamine(0.822 g, 9.15 mmol) and mercaptoacetic acid(0.64 mL, 9.15 mmol) in toluene(50 mL) was dehydrated under reflux for 2 h. The reaction mixture was allowed to cool to room temperature and evaporated to dryness. The residue was purified by flash column chromatography on silica gel to give 2.22 g(97 %) of 3-(2-dimethylaminoethyl)-2-(3-pyridyl)-thiazolidin-4-one.

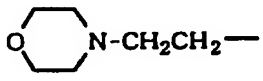
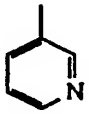
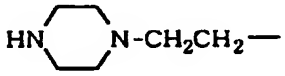
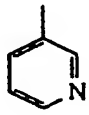
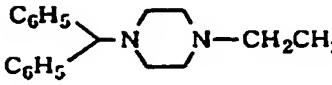
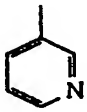
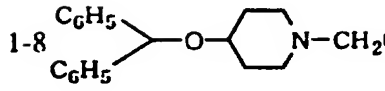
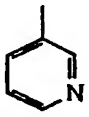
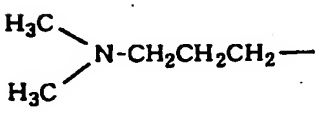
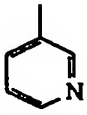
The intermediate compounds of formula(II) as shown in Table 1 were prepared in the same manner as described in EXAMPLE 1.

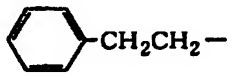
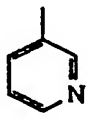
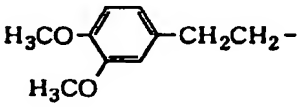
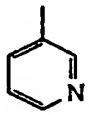
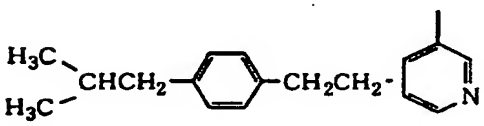
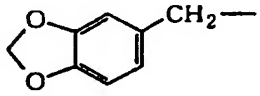
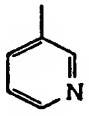
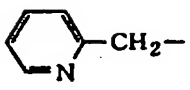
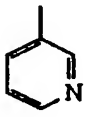
Table 1

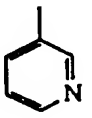
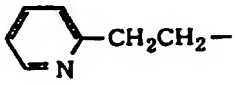
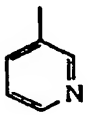
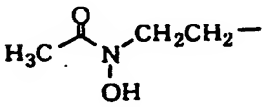
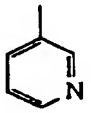
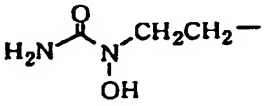
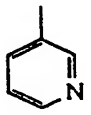
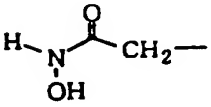
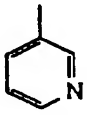
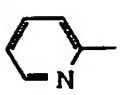
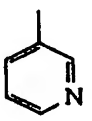


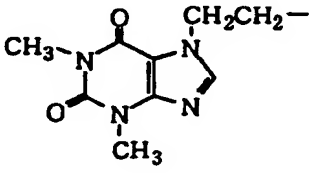
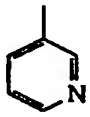
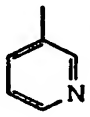
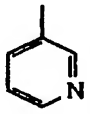
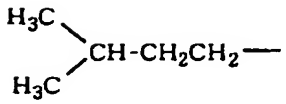
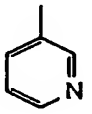
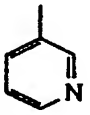
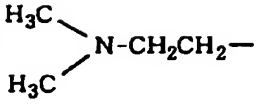
(II)

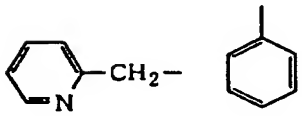
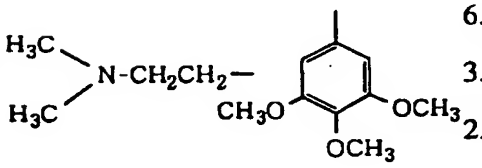
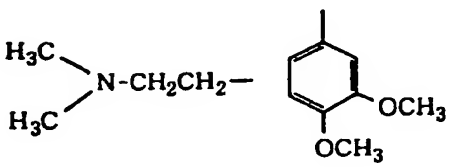
Example	T	Q	^{1}H NMR(300 MHz, $CDCl_3$) δ
1-1			8.63(m, 1H), 8.56(d, J=2.1Hz, 1H), 7.68 (m, 1H), 7.36(m, 1H), 5.93(s, 1H), 3.85~3.77(m, 3H), 2.74~ 2.69(m, 1H), 2.48~2.44(m, 1H), 2.29~2.21(m, 1H), 2.15(s, 6H)
1-2			8.62(m, 1H), 8.55(m, 1H), 7.68(m, 1H), 7.38(m, 1H), 5.98(s, 1H), 3.65 ~3.85(m, 2H), 2.60~2.79(m, 2H), 2.33~2.57(m, 5H), 0.97(t, J=7.2Hz, 6H)
1-3			8.62(m, 1H), 8.60(m, 1H), 7.66(m, 1H), 7.35(m, 1H), 5.94(s, 1H), 3.84(m, 1H), 3.78(m, 2H), 2.74(m, 2H), 2.41(m, 5H), 1.74(m, 4H)
1-4			8.62(m, 1H), 8.55(m, 1H), 7.67(m, 1H), 7.35(m, 1H), 5.98(s, 1H), 3.72 ~3.88(m, 3H), 2.78(m, 1H), 2.51 (m, 1H), 2.29(m, 5H), 1.54(m, 4H), 1.42(m, 2H)

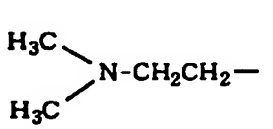
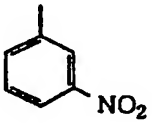
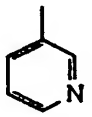
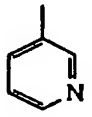
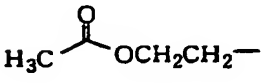
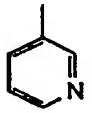
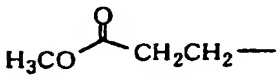
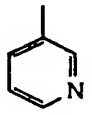
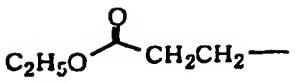
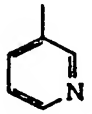
Example	T	Q	^{1}H NMR(300 MHz, $CDCl_3$) δ
1-5			8.63(m, 1H), 8.55(m, 1H), 7.68(m, 1H), 7.36(m, 1H), 5.89(s, 1H), 3.74~3.87(m, 3H), 3.67(m, 4H), 2.78(m, 1H), 2.48(m, 1H), 2.37(m, 5H)
1-6			8.63(m, 1H), 8.55(m, 1H), 7.68(m, 1H), 7.36(m, 1H), 5.92(s, 1H), 3.82(m, 1H), 3.78(m, 2H), 2.87(m, 4H), 2.77(m, 1H), 2.50(m, 1H), 2.35(m, 5H)
1-7			8.57(m, 1H), 8.52(m, 1H), 7.64(m, 1H), 7.10~7.44(m, 1H), 5.93(s, 1H), 4.21(s, 1H), 3.77(m, 3H), 2.73(m, 1H), 2.55(m, 1H), 2.39(m, 9H)
1-8			
1-9			8.63(m, 1H), 8.56(m, 1H), 7.67(m, 1H), 7.35(m, 1H), 5.71(s, 1H), 3.77(m, 2H), 3.68(m, 1H), 2.74(m, 1H), 2.24(m, 1H), 2.16(s, 6H), 1.70(m, 1H), 1.58(m, 1H)

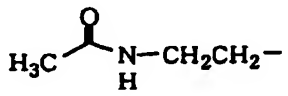
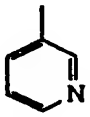
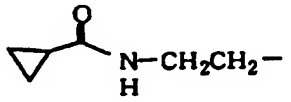
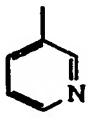
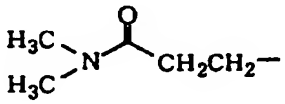
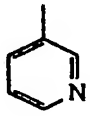
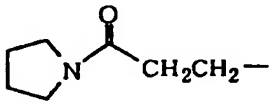
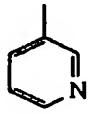
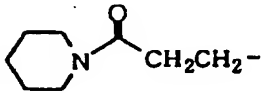
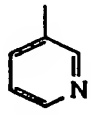
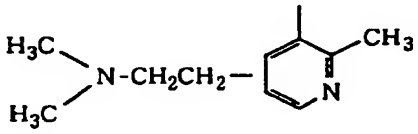
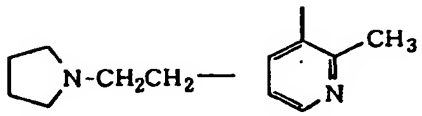
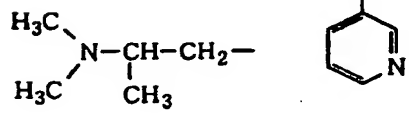
Example	T	Q	^{1}H NMR(300 MHz, $CDCl_3$) δ
1-10			8.61(m, 1H), 8.53(m, 1H), 8.46(m, 1H), 7.64(m, 2H), 7.34(m, 1H), 7.19(m, 2H), 5.54(s, 1H), 4.02(m, 1H), 3.70(m, 2H), 2.80~3.20(m, 3H)
1-11			8.61(m, 1H), 8.41(m, 1H), 7.57(m, 1H), 7.33(m, 1H), 6.80(d, J=8.1Hz, 1H), 6.64 (m, 1H), 6.62(s, 1H), 5.25(s, 1H), 3.90 (m, 1H), 3.87(s, 3H), 3.85(s, 3H), 3.75 (m, 2H), 2.85(m, 2H), 2.68(m, 1H)
1-12			
1-13			8.63(m, 1H), 8.44(d, J=1.8Hz, 1H), 7.64 (m, 1H), 7.34(m, 1H), 6.70(d, J=7.8Hz, 1H), 6.62(s, 1H), 6.45(d, J=7.8Hz, 1H), 5.95(s, 2H), 5.42(s, 1H), 4.25(ABq, $\Delta\nu$ =467, J_{AB}= 15.0Hz, 2H), 3.84(ABq, $\Delta\nu$ =40.0, J_{AB}= 15.6Hz, 2H)
1-14			8.60(m, 1H), 8.51(m, 1H), 7.60~ 7.76(m, 2H), 7.34(m, 1H), 7.19(m, 1H), 5.83(s, 1H), 5.04(d, Jgem= 15.3Hz, 1H), 3.90 (m, 2H), 3.81(d, Jgem=15.3Hz, 1H)

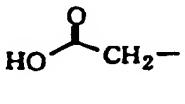
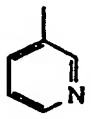
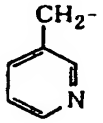
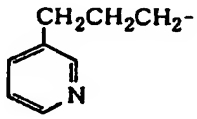
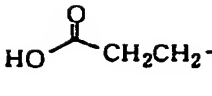
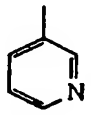
Example	T	Q	^{1}H NMR(300 MHz, $CDCl_3$) δ
1-15	$CH_3CH_2CH_2$-O—		
1-16			
1-17			
1-18			
1-19			8.63(m, 1H), 8.49(m, 1H), 7.34(m, 1H), 7.24(m, 1H), 5.89(s, 1H), 4.25(ABq, 2H), 3.98(ABq, 2H)
1-20			8.61(m, 1H), 8.46(m, 1H), 8.22(m, 1H), 8.10(d, J=8.4Hz, 1H), 7.67(m, 2H), 7.25 (m, 1H), 7.01(m, 1H), 6.87(s, 1H), 3.95 (ABq, $\Delta\nu$ = 56.7Hz, J_{AB}=16,2Hz, 2H)

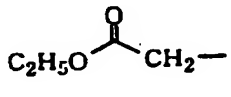
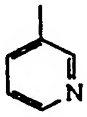
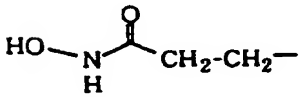
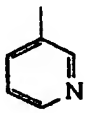
Example	T	Q	^{1}H NMR(300 MHz, $CDCl_3$) δ
1-21			8.52(m, 1H), 8.40(m, 1H), 7.52(m, 1H), 7.51(s, 1H), 7.18(m, 1H), 5.45 (s, 1H), 4.62(m, 1H), 4.37(m, 1H), 3.87(m, 1H), 3.80(dd, 2H), 3.60(s, 3H), 3.40(m, 1H), 3.34(s, 3H)
1-22	OH		8.57(s, 2H), 8.05(s, 1H), 7.78(d, J= 7.8Hz, 1H), 7.33(m, 2H), 5.79(s, 1H), 3.66(s, 2H)
1-23	CH_3-$(CH_2)_3$—		8.64(m, 1H), 8.55(m, 1H), 7.68(m, 1H), 7.37(m, 1H), 5.65(d, J=1.5Hz, 1H), 3.70 (m, 1H), 2.64(m, 1H), 1.44(m, 2H), 1.27 (m, 2H), 0.87(t, J=7.5Hz, 3H)
1-24			
1-25	CH_3—		
1-26		CH_3-$(CH_2)_7$—	4.78(dd, J=6.3, 1.8Hz, 1H), 3.82(td, J= 7.2, 7.2Hz, 1H), 3.54(ABq, 2H), 3.07(td, J=7.2Hz, 2H), 2.35(m, 2H), 2.26(s, 6H), 1.92(m, 1H), 1.63(m, 1H), 1.18~1.46(m, 12H), 0.89(t, J=6.6Hz, 3H)

Example	T	Q	^{1}H NMR(300 MHz, $CDCl_3$) δ
1-27	CH_3—	CH_3-$(CH_2)_7$—	4.57(m, 1H), 3.56(dd, 2H), 2.90(s, 3H), 1.84~1.99(m, 1H), 1.57~1.80 (m, 1H), 1.05~1.55(m, 12H), 0.89(t, J=6.6Hz, 3H)
1-28	CH_3—	CH_3-$(CH_2)_5$—	4.58(m, 1H), 3.57(ABq, 2H), 2.89 (s, 3H), 1.90(m, 1H), 1.72(m, 1H), 1.32(m, 8H), 0.89(t, J=6.6Hz, 3H)
1-29	CH_3—	CH_3-$(CH_2)_2$—	4.58(m, 1H), 3.54(ABq, $\Delta\nu$ =28, JAB= 15.6Hz, 2H), 2.90(s, 3H), 1.83~1.99(m, 1H), 1.61~1.79(m, 1H), 1.32~1.52(m, 2H), 0.98(t, J=7.2Hz, 3H)
1-30			
1-31			6.52(s, 2H), 5.80(s, 1H), 3.86(s, 9H), 3.79(m, 1H), 3.77(m, 2H), 2.86(m, 1H), 2.46(m, 1H), 2.34(m, 1H), 2.21(s, 6H)
1-32			

Example	T	Q	1H NMR(300 MHz, CDCl3) δ
1-33			
1-34			
1-35			
1-36			8.61(m, 2H), 7.68(m, 1H), 7.37(m, 1H), 5.81(d, J=0.9Hz, 1H), 3.76(m, 3H), 3.68 (s, 3H), 3.06(m, 1H), 3.71(m, 1H), 2.46 (m, 1H)
1-37			8.63(m, 2H), 7.70(m, 1H), 7.38(m, 1H), 5.81(s, 1H), 3.78(m, 3H), 3.67(s, 3H), 3.05(m, 1H), 2.71(m, 1H), 2.46(m, 1H)
1-38			8.61(m, 1H), 8.57(m, 1H), 7.82(m, 1H), 7.45(m, 1H), 5.90(d, J=1.2Hz, 1H), 4.02 (q, J=7.2Hz, 2H), 3.92 (dd, J=15.6, 1.2Hz, 1H), 3.67(d, J=15.6Hz, 1H), 3.61~3.73 (m, 1H), 2.87(m, 1H), 2.54(m, 1H), 2.40(m, 1H), 1.15(t, J=7.2Hz, 3H)

Example	T	Q	^{1}H NMR(300 MHz, $CDCl_3$) δ
1-39			
1-40			
1-41			
1-42			
1-43			
1-44			8.47(dd, J=4.8, 1.2Hz, 1H), 7.45 (dd, J= 7.8, 1.5Hz, 1H), 7.21(m, 1H), 6.21(s, 1H), 3.85(td, J=7.8, 1.8Hz, 1H), 3.72(s, 2H), 2.72(m, 1H), 2.59(s, 3H), 2.52(m, 1H), 2.31(m, 1H), 2.13(s, 3H)
1-45			
1-46			8.63(m, 1H), 8.56(d, J=2.1Hz, 1H), 7.68 (m, 1H), 7.36(m, 1H), 5.93(s, 1H), 3.85~3.77(m, 3H), 2.74~2.69 (m, 1H), 2.48~2.44(m, 1H), 2.15(s, 6H), 1.22(d, J=7.2Hz, 3H)

Example	T	Q	^{1}H NMR(300 MHz, $CDCl_3$) δ
1-47			DMSO-d ; 8.60(d, J=1.8Hz, 1H), 8.55 (dd, J=4.2, 1.8Hz, 1H), 7.85(m, 1H), 7.43(m, 1H), 5.85(s, 1H), 3.85 (ABq, $\Delta\nu$ =72, J_{AB}=15.6Hz, 2H), 3.74(ABq, $\Delta\nu$ =219, J_{AB}= 17.Hz, 2H)
1-48	CH_3—		8.53(m, 2H), 7.55(d, J=7.8Hz, 1H), 7.25 m, 1H), 4.79(m, 1H), 3.17 (ABq, 2H), 3.04(s, 3H)
1-49	CH_3—		8.47(m, 2H), 7.50(m, 1H), 7.23(m, 1H), 4.60(dd, J=1.8, 5.1Hz), 3.55 (m, 2H), 2.86(s, 3H), 2.68(t, J= 5.7Hz, 2H), 1.62~1.98(m, 4H)
1-50			12.34(brs, 1H), 8.60(m, 1H), 8.58 (m, 1H), 7.83(m, 1H), 7.45(m, 1H), 5.91(d, J=1.2Hz, 1H), 3.92 (dd, J=15.6, 1.2Hz, 1H), 3.67(d, J=15.6Hz, 1H), 3.63(m, 1H), 2.83(m, 1H), 2.54(m, 1H), 2.29(m, 1H)

Example	T	Q	^{1}H NMR(300 MHz, $CDCl_3$) δ
1-51			8.61(m, 1H), 8.56(m, 1H), 7.86(m, 1H), 7.42(m, 1H), 5.86(s, 1H), 4.14(d, J= 17.4Hz, 1H), 4.02(d, J= 15.6Hz, 1H), 3.01(q, J=7.2Hz, 2H), 3.74(d, J=15.6Hz, 1H), 3.58(d, J= 17.4Hz, 1H), 1.13(t, J= 7.2Hz, 3H)
1-52			10.51(s, 1H), 8.80(s, 1H), 8.59(m, 2H), 7.82(m, 1H), 7.46(m, 1H), 5.88(s, 1H), 3.93(d, J=15.3Hz, 1H), 3.63(m, 1H), 3.67(d, J=15.3Hz, 1H), 2.80(m, 1H), 2.29(m, 1H), 2.07(m, 1H)

EXAMPLE 2.

Preparation of 3-(2-dimethylaminoethyl)-5-(α-hydroxybenzyl)-2-(3-pyridyl)-thiazolidin-4-one

< Method A >

To a solution of diisopropylamine (0.142 mL, 0.796 mmol) in tetrahydrofuran (10 mL) was added *n*-BuLi (1.6 M solution, 0.5 mL, 0.80 mmol) at -78 ℃. After stirried for 1 h. To the reaction mixture was added 3-(2-dimethylaminoethyl)-2-(3-pyridyl)-thiazolidin-4-one(0.20 g, 0.796 mmol) dissolved in tetrahydrofuran(1.5 mL). After stirried for 30 min, to the reaction mixture was added benzaldehyde(98 μl, 0.950 mmol) and stirred for 1 h and allowed to warm to room temperature. The reaction mixture was poured into brine(2 mL) and it was then extracted by using ethyl acetate(30 mL).

The ethyl acetate phase was dried over anhydrous magnesium sulfate and evaporated to dryness. The residure was purified by flash column chromatography on silica gel to give 0.253 g(89 %) of 3-(2-dimethylaminoethyl)-5-(α-hydroxybenzyl)-2-(3-pyridyl)-thiazolidin-4-one.

^{1}H NMR(300 MHz, $CDCl_3$) δ : 8.62(m, 2H), 7.81(m, 1H), 7.36(m, 1H), 7.29~7.26 (m, 5H), 5.84(s, 1H), 5.18(s, 1H), 4.52(s, 1H), 4.20 (m, 1H), 2.75~2.35(m, 3H), 2.17(s, 6H).

< Method B >

To a solution of 3-(2-dimethylaminoethyl)-2-(3-pyridyl)-thiazolidin-4-one (0.35 g, 1.39 mmol) in carbon tetrachloride (30 mL) was added *N*-bromosuccinimide (0.260 g, 1.46 mmol) and benzoyl peroxide(1 mg). The reaction mixture was heated under reflux for 5 h in the dark and filtered off precipitate. The filtrate was evaporated to give crude 5-bromo-3-(2-dimethylaminoethyl)-2-(3-pyridyl)-thiazolidin-4-one.

^{1}H NMR(300 MHz, $CDCl_3$) δ : 8.62~8.58(m, 2H), 7.70(d, *J*=8.1Hz, 1H), 7.36~7.33 (m, 1H), 5.94(s, 1H), 5.21(s, 1H), 4.68~4.80(m, 1H),

2.82(m, 1H), 2.61~2.43(m, 2H), 2.28(s, 6H).

To a solution of Zn(0.136 g, 2.09 mmol), CuBr(15 mg, 0.670 mmol) and diethylaluminium chloride (0.184 mg, 1.53 mmol) in mixture of tetrahydrofuran and hexane (10 mL/10 mL) was slowly added 5-bromo-3-(2-dimethylaminoethyl)-2-(3-pyridyl)-thiazolidin-4-one and benzaldehyde (0.162 g, 1.53 mmol) dissolved in tetrahydrofuran at -20 ℃ for 5 min. After stirred for 2 h, to the reaction mixture was added pyridine (1 mL) warmed to room temperature, diluted with water (10 mL) and extracted with ethyl acetate(80 mL). The combined organic phase was dried over anhydrous magnesium sulfate, filtered, and evaporated to dryness. The residue was purified by flash column chromatography on silica gel to give 0.468 g (94 %) of 3-(2-dimethylaminoethyl)-5-(α-hydroxybenzyl)-2-(3-pyridyl)-thiazolidin-4-one.

EXAMPLE 3.

Preparation of 3-(2-dimethylaminoethyl)-5-phenylmethylene-2-(3-pyridyl)-thiazolidin-4-one.

< Method A >

A solution of 3-(2-dimethylaminoethyl)-2-(3-pyridyl)-thiazoldin-4-one(0.130 g, 0.517 mmol) in tetrahydrofuran(10 mL) was cooled to 0 ℃ and added potassium hydride(51 mg, 1.29 mmol). After stirred for 5 min, to the reaction mixture was added benzaldehyde(64 μl, 0.621 mmol) and warmed to room temperature. After stirred at room temperature for 1h, the reaction mixture was cooled to 0 ℃, poured into water(0.2 mL), and extrated with ethyl acetate(20 mL). The combined organic phase was dried over anhydrous magnesium sulfate, filtered, and evaporated to dryness. The residue was purified by flash column chromatography on silica gel to give 0.166 g (95 %) of 3-(2-dimethylaminoethyl)-5-phenylmethylene-2-(3-pyridyl)-thiazolidin-4-one.

^{1}H NMR(300 MHz, $CDCl_3$) δ : 8.65~8.61(m, 2H), 7.66(d, J=8.1Hz, 1H), 7.53(s, 1H), 7.44~7.34(m, 5H), 6.18(s, 1H), 4.08~3.97(m, 1H), 2.78~2.82(m, 1H), 2.63~2.53(m, 1H),

2.40–2.35(m, 1H), 2.19(s, 6H).

< Method B >

To a solution of 3-(2-dimethylaminoethyl)-2-(3-pyridyl)-thiazoldin-4-one (0.126 g, 0.501 mmol) in acetic acid(10 mL) was added sodium acetate (0.165 g, 20.1 mmol) and benzaldehyde(80 mg, 0.751 mmol). The reaction mixture was heated under reflux for 8 h and evaporated to dryness. The residue was dissolved in water(5 mL) and extrated with ethyl acetate(30 mL). The combined organic phase was dried over anhydrous magnesium sulfate, filtered, and evaporated to dryness. The residue was purified by flash column chromatography on silica gel to give 0.144 g (85 %) of 3-(2-dimethylaminoethyl)-5-phenylmethylene-2-(3-pyridyl)-thiazolidin-4-one.

< Method C >

To a solution of 3-(2-dimethylaminoethyl)-5-(α-hydroxybenzyl)-2-(3-pyridyl)-thiazolidin-4-one(0.20 g) in toluene(10 mL) was added *p*-toluenesulfonic acid(10 mg). The reaction mixture was dehydrated under reflux for 2 h, cooled to room temperature, and evaporated. The residue was purified by flash column chromatography on silica gel to give 0.188 g (99 %) of 3-(2-dimethylaminoethyl)-5-phenylmethylene-2-(3-pyridyl)-thiazolidin-4-one.

< Method D >

A solution of 3-(2-dimethylaminoethyl)-5-(α-hydroxybenzyl)-2-(3-pyridyl)-thiazoldin-4-one(0.40 g) dissolved in 28 % HCl-ethanol (5 mL) was stirred for 10 min at room temperature and evaporated. The residue was purified by flash column chromatography on silica gel to give 0.345 g (91 %) of 3-(2-dimethylaminoethyl)-5-phenylmethylene-2-(3-pyridyl)-thiazolidin-4-one.

EXAMPLE 4.

Preparation of 3-(2-dimethylaminoethyl)-5-phenylmethylene-2-(3-pyridyl)-thiazolidin-4-one hydrochloride salt (Compound No. 1).

A solution of 3-(2-dimethylaminoethyl)-5-phenylmethylene-2-(3-pyridyl)-thiazolidin-4-one (0.50g) dissolved in 28 % HCl-ethanol (2 mL) was stirred for 3 h at room

temperature and filtered the precipitate. The precipitate was dried under vac. to give 0.537 g(97 %) of 3-(2-dimethylaminoethyl)-5-phenylmethylene-2-(3-pyridyl)-thiazolidin-4-one hydrochloride salt.

^{1}H NMR(300 MHz, DMSO-d_6) δ : 9.70(s, 1H), 8.79(s, 1H), 8.69(d, J=4.5Hz, 1H), 7.97(d, J=8.1Hz, 1H), 7.60~7.55(m, 6H), 6.39(s, 1H), 4.20~4.12(m, 1H), 3.21~3.00(m, 3H), 2.82(d, J=3.9Hz, 6H).

The compounds of formula(I), wherein R^4, R^5, R^6, R^7 or R^8 is an hydroxyl group, can be prepared in the following EXAMPLE 5, introducing protecting group such as methoxyethoxymethyl group.

EXAMPLE 5.

Preparation of 3-(2-*N*, *N*-dimethylaminoethyl)-5-(3,5-dimethyl-4-hydroxy-phenylmethylene)-2-(3-pyridyl)-thiazolidin-4-one hydrochloride salt (Compound No. 10)

A solution of 3,5-dimethyl-4-hydroxybenzaldehyde (10.0 g, 66.6 mmol) in tetrahydrofuran(100 mL) was cooled to 0 ℃ and added 80 % NaH (2.40 g, 79.9 mmol). After stirred for 10 min at 0 ℃, to the reaction mixture was added 2-methoxyethoxymethyl chloride (11.6 g, 93.2 mmol) and warmed to room temperature. After stirred for 4 h, the reaction mixture was cooled to 0 ℃ and added methanol (10 mL). When no more evolution of hydrogen gas the reaction mixture was warmed to room temperature added water(20 mL) and extracted with ethyl acetate(2 x 100 mL). The combined organic phase was dried over anhydrous magnesium sulfate, filtered, and evaporated to dryness. The residue was purified by flash column chromatography on silica gel to give 13.6 g(86%) of 3,5-dimethyl-4-(2-methoxyethoxymethyloxy)-benzaldehyde.

^{1}H NMR(300 MHz, $CDCl_3$) δ : 9.87(s, 1H), 7.55(s, 2H), 5.12(s, 2H), 3.95(t, J=4.5Hz, 2H), 3.60(t, J=4.5Hz, 2H), 3.39(s, 3H), 2.35 (s, 6H)

To a solution of 3-(2-*N,N*-dimethylaminoethyl)-2-(3-pyridyl)-thiazolidin-4-one (1.00 g, 3.98 mmol) in tetrahydrofuran(50 mL) was added lithium diisopropylamide (1.5M solution, 3.18 mL) at -78 ℃ and stirred for 10 min. To the reaction mixture was slowly added 3,5-dimethyl-4-(2-methoxyethoxymethyloxy)-benzaldehyde(1.13 g, 4.77 mmol) dissolved in tetrahydrofuran(5 mL). After stirred at -78 ℃ for 2 h, to the reaction mixture was added acetic acid(2 mL) and warmed to room temperature. The reaction mixture was neutralized with saturated sodium bicarbonate solution and extracted with ethyl acetate(3 x 30 mL). The combined organic phase was dried over anhydrous magnesium sulfate, filtered, and evaporated to dryness. The residue was dissolved in 30% HCl-ethanol solution(5 mL), stirred for 3 h and then neutralized with saturated sodium bicarbonate solution and extracted with ethyl acetate (2 x 50 mL). The combined organic phase was dried over anhydrous magnesium sulfate, filtered, and evaporated to dryness. The residue was purified by flash column chromatography on silica gel to give 1.32 g(87 %) of 3-(2-*N,N*-dimethylaminoethyl)-5-(3,5-dimethyl-4-hydroxy-phenylemthylene)-2-(3-pyridyl)-thiazolidin-4-one.

^{1}H NMR(300 MHz, $CDCl_3$) δ : 8.63~8.61(m, 2H), 7.75(m, 1H), 7.54(s, 1H), 7.35 (m, 1H), 7.21(s, 2H), 6.17(s, 1H), 4.15(m, 1H), 2.85 (m, 1H), 2.60(m, 1H), 2.38(m, 1H), 2.18(s, 6H)

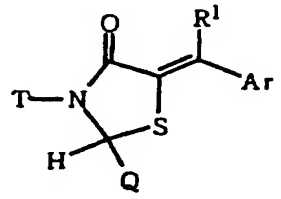
To a solution of 3-(2-*N,N*-dimethylaminoethyl)-5-(3,5-dimethyl-4-hydroxy-phenylemthylene)-2-(3-pyridyl)-thiazolidin-4-one(1.32 g, 3.44 mmol) in ethanol(4 mL) was added 30 % HCl-ethanol solution(0.94 mL) and stirred at room temperature for 30 min. To the reaction mixture was added ethyl acetate(30 mL), filtered, and dried to give 1.49 g(95 %) of 3-(2-*N,N*-dimethylaminoethyl)-5-(3,5-dimethyl-4-hydroxy-phenylemthylene)-2-(3-pyridyl)-thiazolidin-4-one hydrochloride salt.

^{1}H NMR(300 MHz, DMSO-d_6) δ : 9.60(brs, 1H), 8.80(s, 1H), 8.68(d, *J*=4.5Hz, 1H), 8.01(m, 1H), 7.61(m, 1H), 7.38(s, 1H), 7.16(s, 2H), 6.26(s, 1H), 4.20(m, 1H), 3.31~3.01(m, 3H), 2.82(d,

J=3.8Hz, 6H), 2.36(s, 6H)

The thiazolidin-4-one derivatives of formula(I) as shown in Table 2 were prepared in the same manner as described in EXAMPLE 1 to EXAMPLE 5.

Table 2



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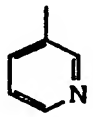
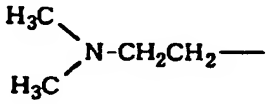
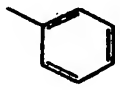
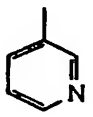
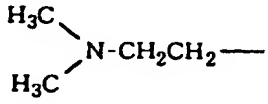
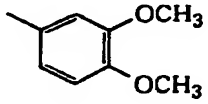
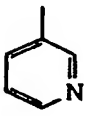
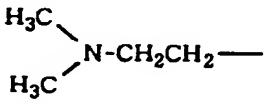
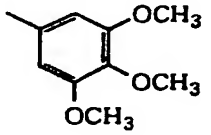
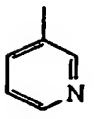
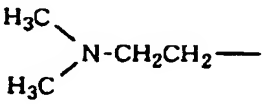
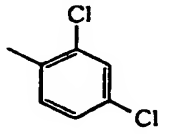
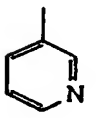
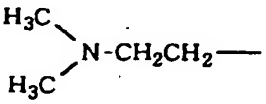
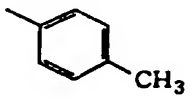
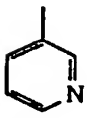
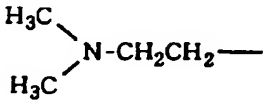
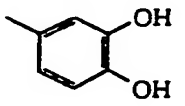
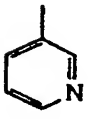
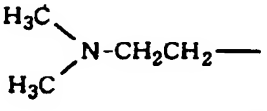
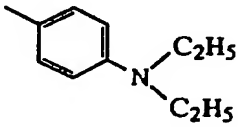
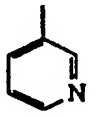
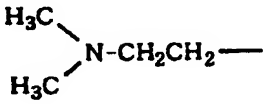
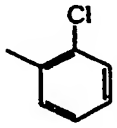
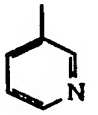
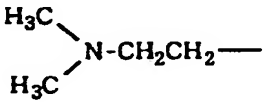
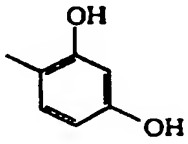
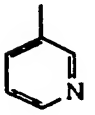
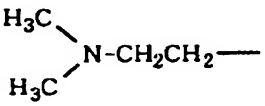
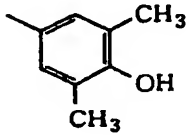
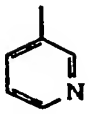
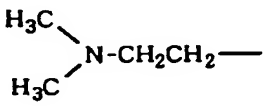
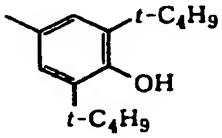
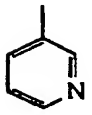
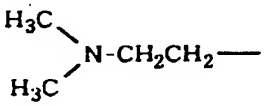
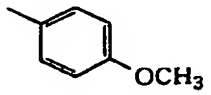
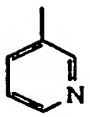
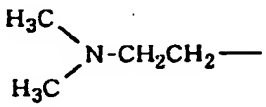
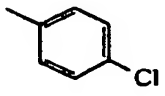
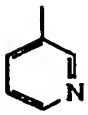
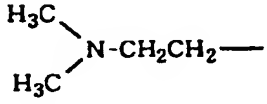
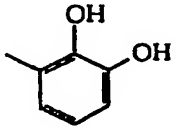
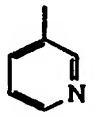
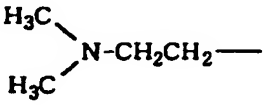
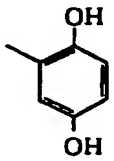
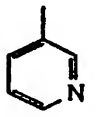
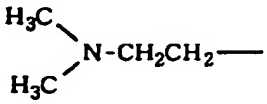
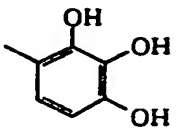
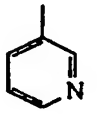
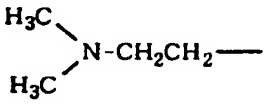
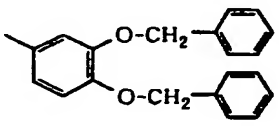
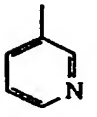
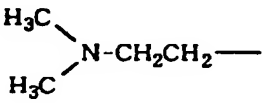
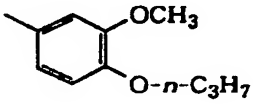
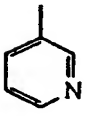
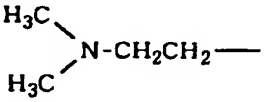
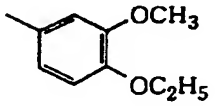
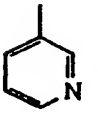
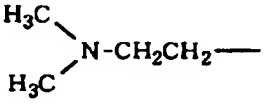
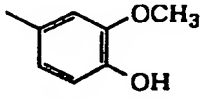
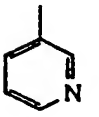
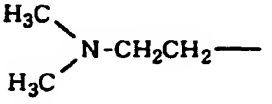
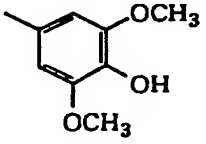
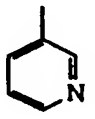
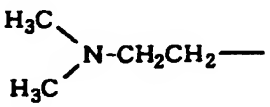
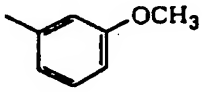
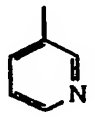
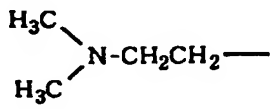
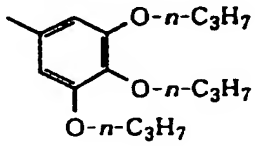
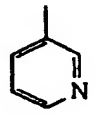
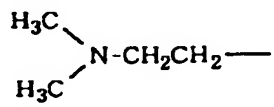
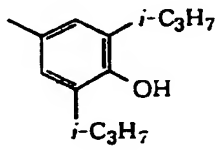
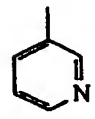
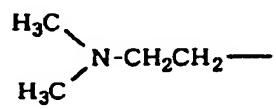
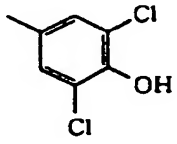
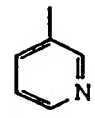
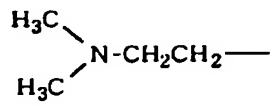
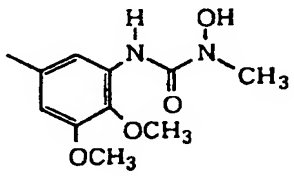
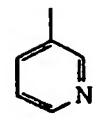
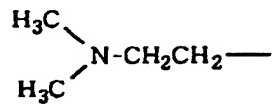
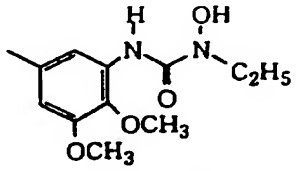
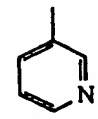
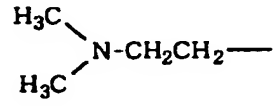
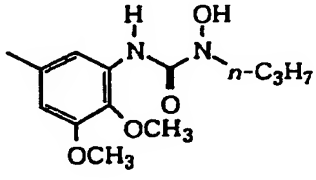
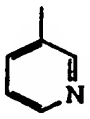
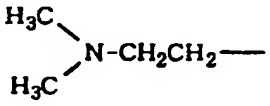
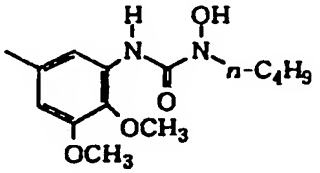
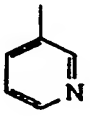
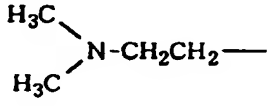
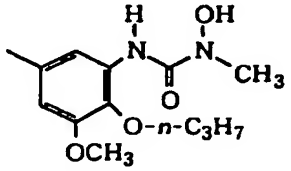
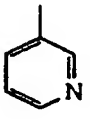
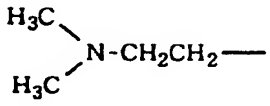
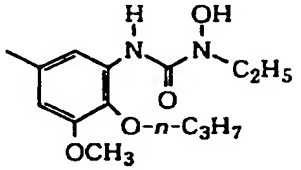
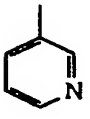
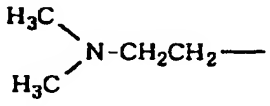
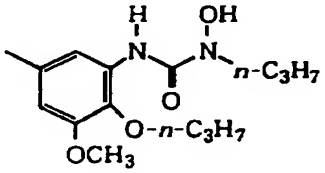
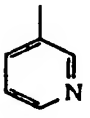
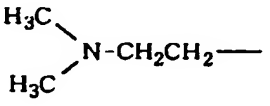
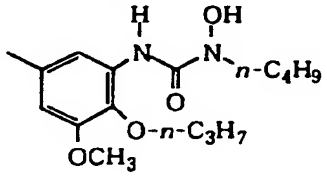
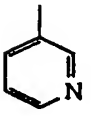
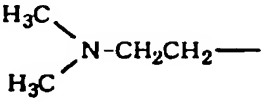
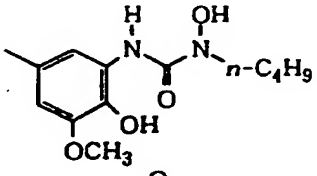
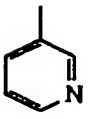
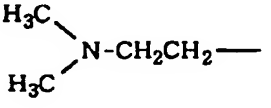
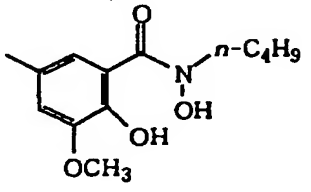
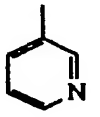
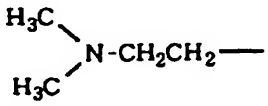
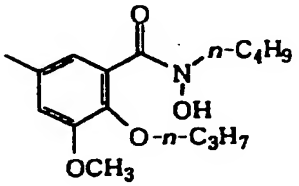
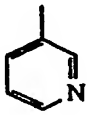
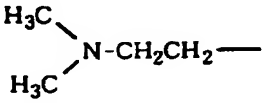
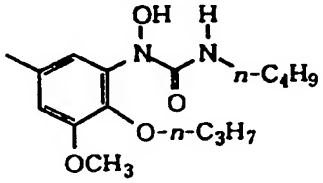
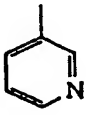
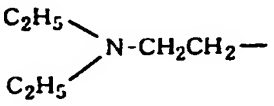
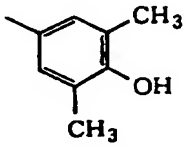
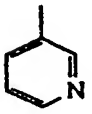
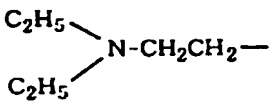
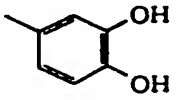
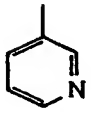
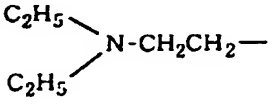
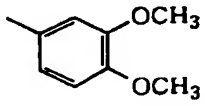
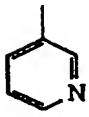
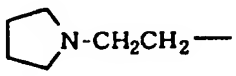
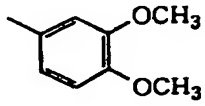
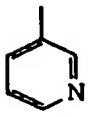
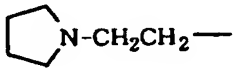
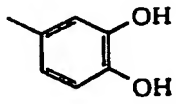
1			H		HCl
2			H		
3			H		
4			H		HCl
5			H		HCl
6			H		HCl
7			H		

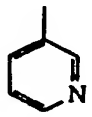
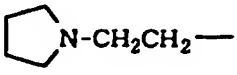
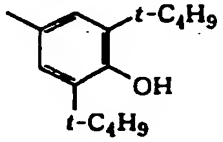
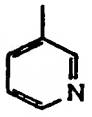
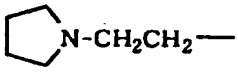
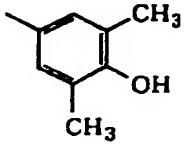
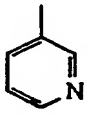
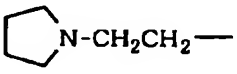
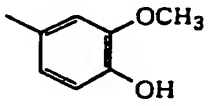
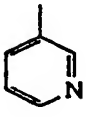
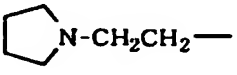
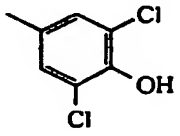
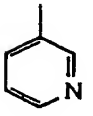
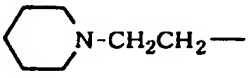
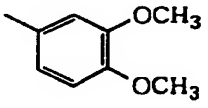
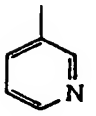
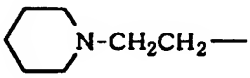
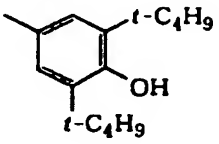
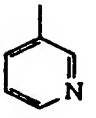
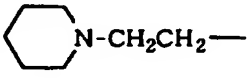
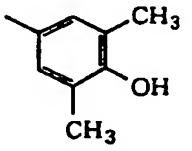
Comp. No.	Q	T	R^1	Ar	Salt
8			H		
9			H		HCl
10			H		HCl
11			H		
12			H		
13			H		
14			H		HCl

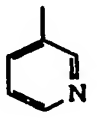
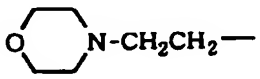
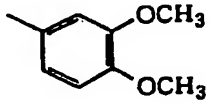
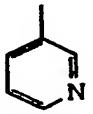
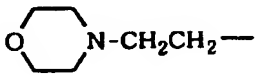
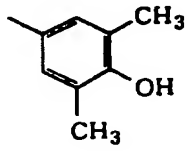
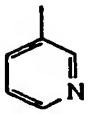
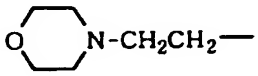
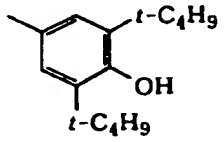
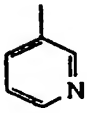
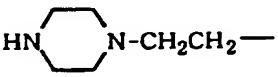
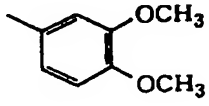
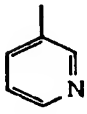
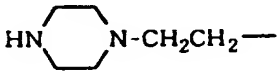
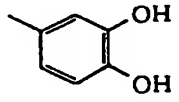
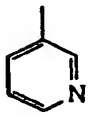
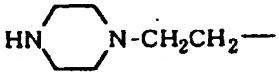
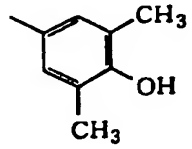
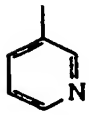
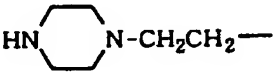
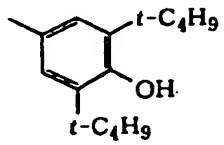
Comp. No.	Q	T	R^1	Ar	Salt
15			H		HCl
16			H		HCl
17			H		
18			H		HCl
19			H		
20			H		HCl
21			H		HCl

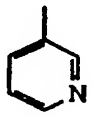
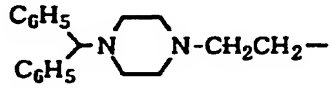
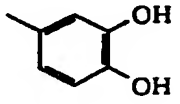
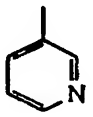
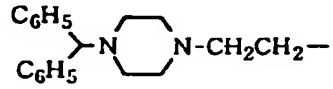
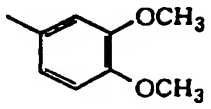
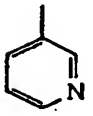
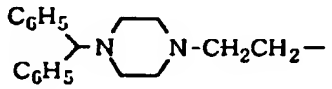
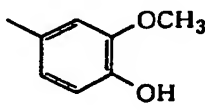
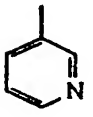
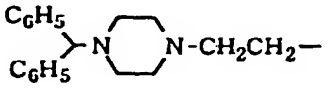
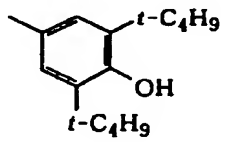
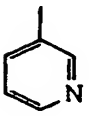
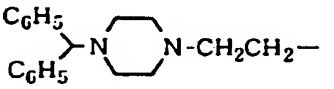
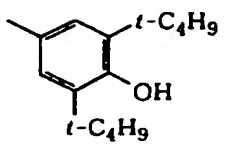
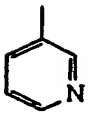
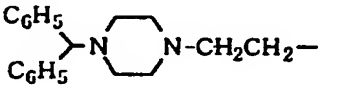
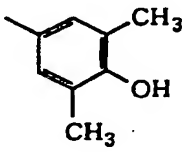
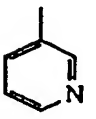
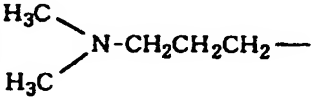
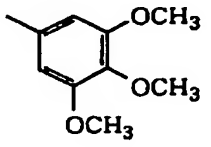
Comp. No.	Q	T	R^1	Ar	Salt
22			H		HCl
23			H		HCl
24			H		
25			H		
26			H		
27			H		
28			H		

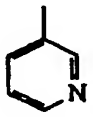
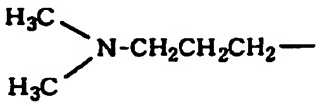
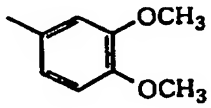
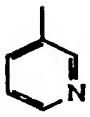
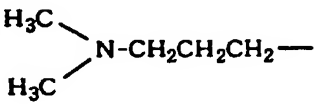
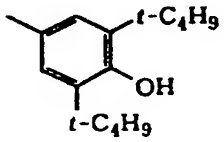
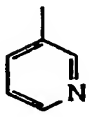
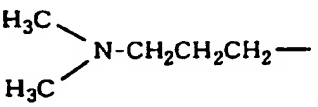
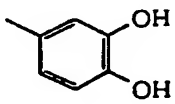
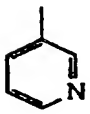
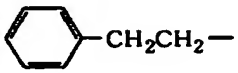
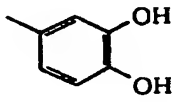
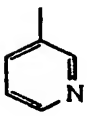
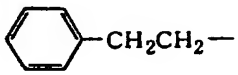
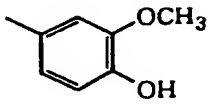
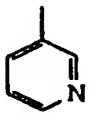
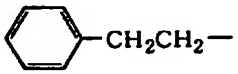
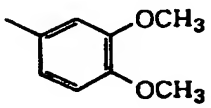
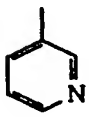
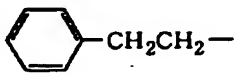
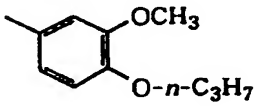
Comp. No.	Q	T	R^1	Ar	Salt
29			H		
30			H		
31			H		
32			H		
33			H		
34			H		
35			H		

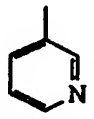
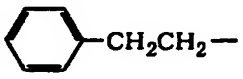
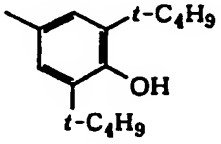
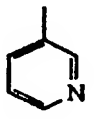
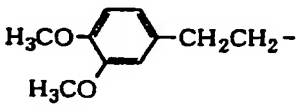
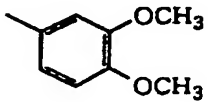
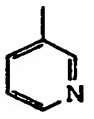
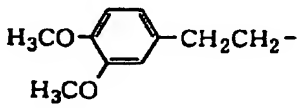
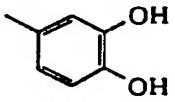
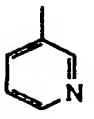
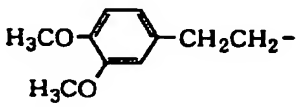
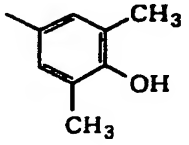
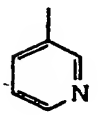
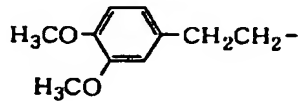
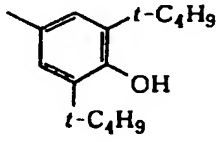
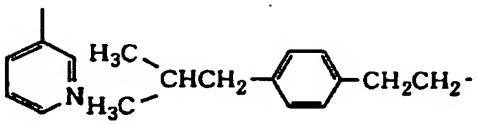
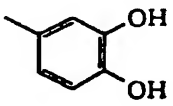
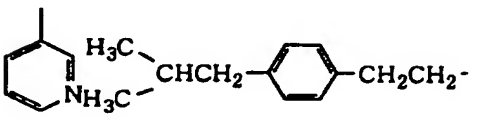
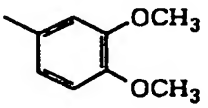
Comp. No.	Q	T	R^1	Ar	Salt
36			H		
37			H		
38			H		
39			H		HCl
40			H		
41			H		
42			H		

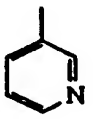
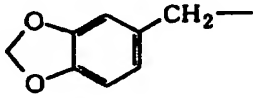
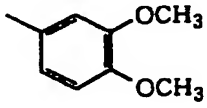
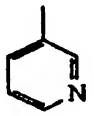
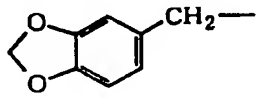
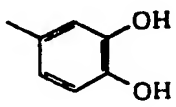
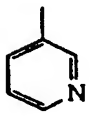
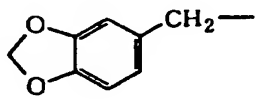
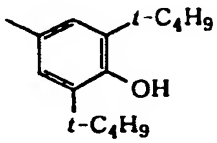
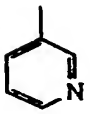
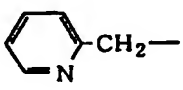
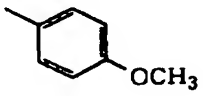
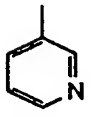
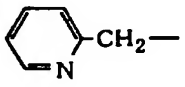
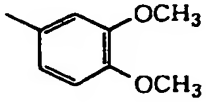
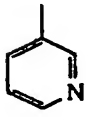
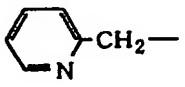
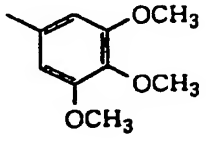
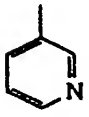
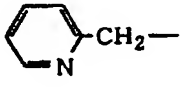
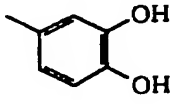
Comp. No.	Q	T	R^1	Ar	Salt
43			H		
44			H		
45			H		
46			H		
47			H		
48			H		
49			H		

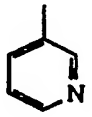
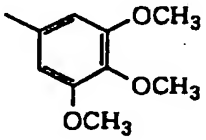
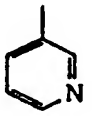
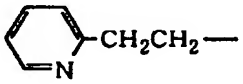
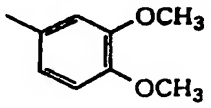
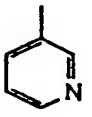
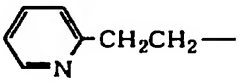
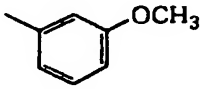
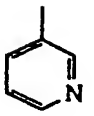
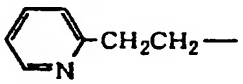
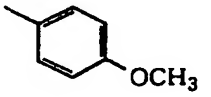
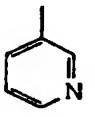
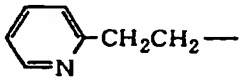
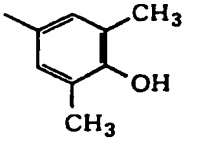
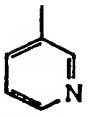
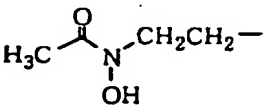
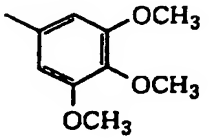
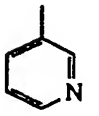
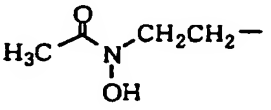
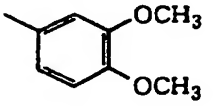
Comp. No.	Q	T	R^1	Ar	Salt
50			H		
51			H		
52			H		
53			H		
54			H		
55			H		
56			H		

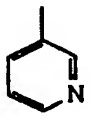
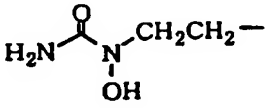
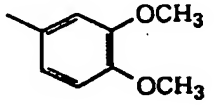
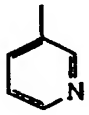
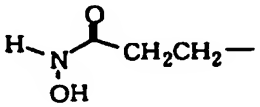
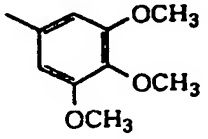
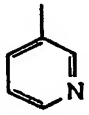
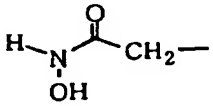
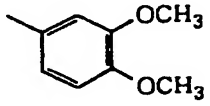
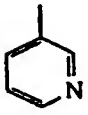
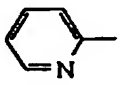
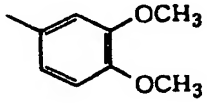
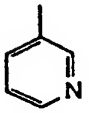
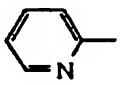
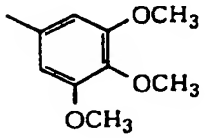
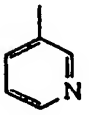
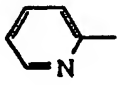
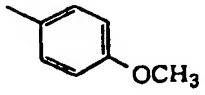
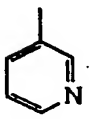
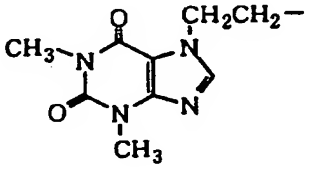
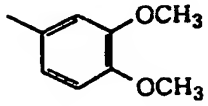
Comp. No.	Q	T	R^1	Ar	Salt
57			H		
58			H		
59			H		
60			H		
61			H		
62			H		
63			H		HCl

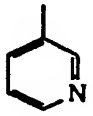
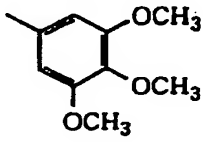
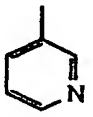
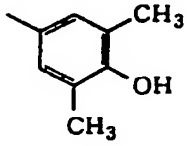
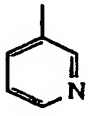
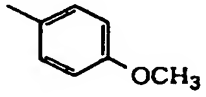
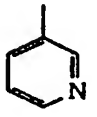
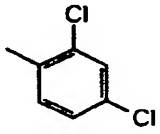
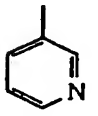
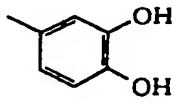
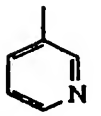
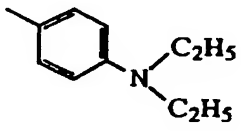
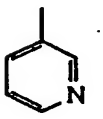
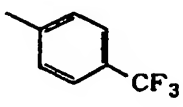
Comp. No.	Q	T	R^1	Ar	Salt
64			H		HCl
65			H		
66			H		
67			H		HCl
68			H		HCl
69			H		HCl
70			H		HCl

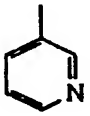
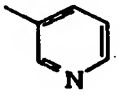
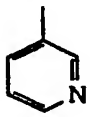
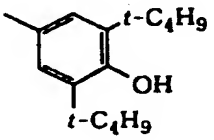
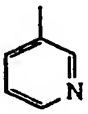
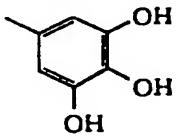
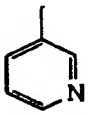
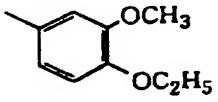
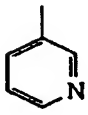
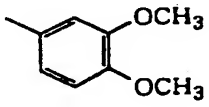
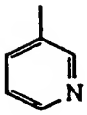
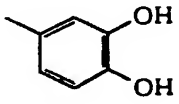
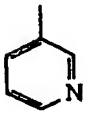
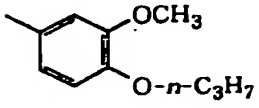
Comp. No.	Q	T	R^1	Ar	Salt
71			H		HCl
72			H		
73			H		HCl
74			H		
75			H		
76			H		
77			H		

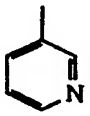
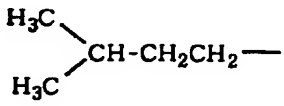
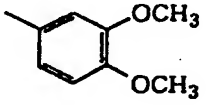
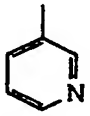
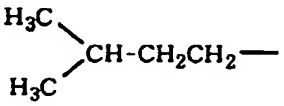
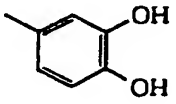
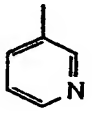
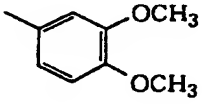
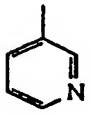
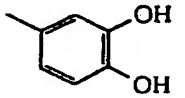
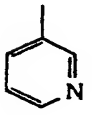
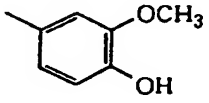
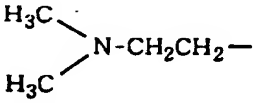
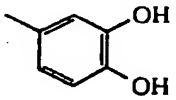
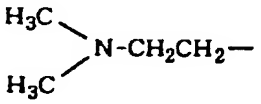
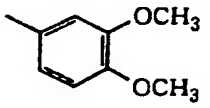
Comp. No.	Q	T	R^1	Ar	Salt
78			H		
79			H		HCl
80			H		HCl
81			H		
82			H		
83			H		
84			H		HCl

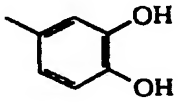
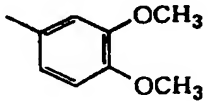
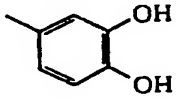
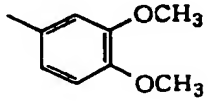
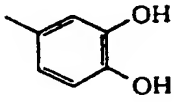
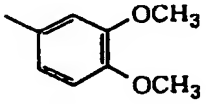
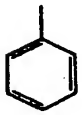
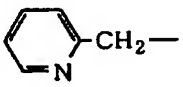
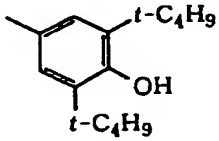
Comp. No.	Q	T	R^1	Ar	Salt
85		$CH_3CH_2CH_2$-O—	H		HCl
86			H		
87			H		
88			H		
89			H		HCl
90			H		
91			H		HCl

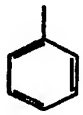
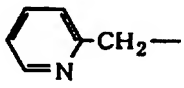
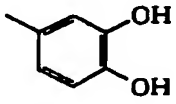
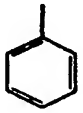
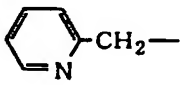
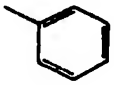
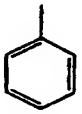
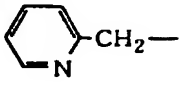
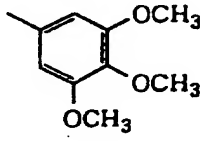
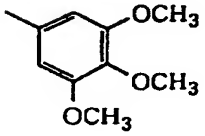
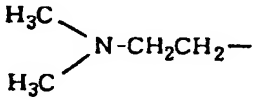
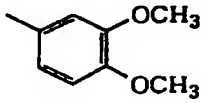
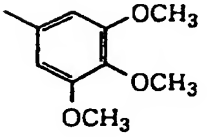
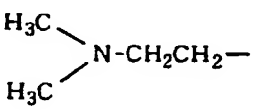
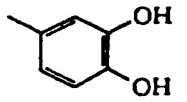
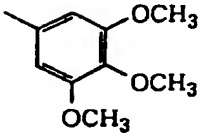
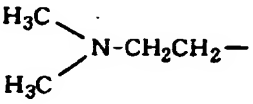
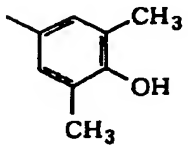
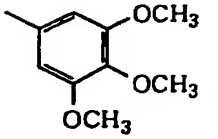
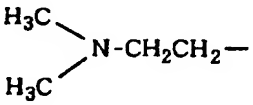
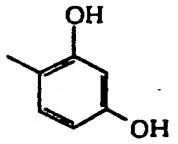
Comp. No.	Q	T	R^1	Ar	Salt
92			H		
93			H		HCl
94			H		
95			H		
96			H		
97			H		
98			H		

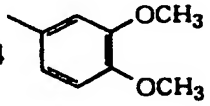
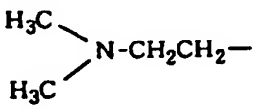
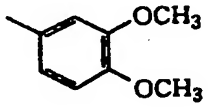
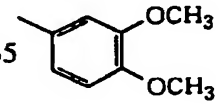
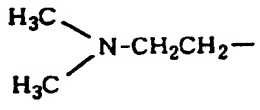
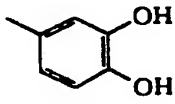
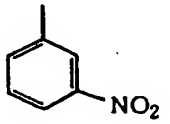
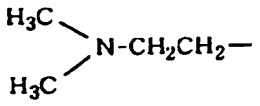
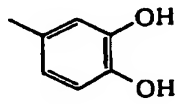
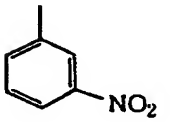
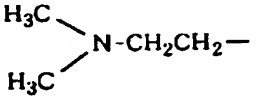
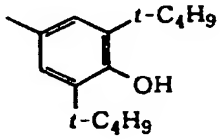
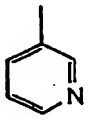
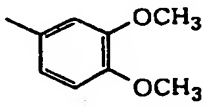
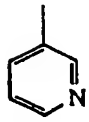
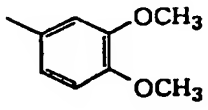
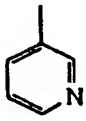
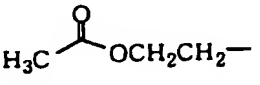
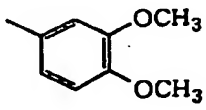
Comp. No.	Q	T	R^1	Ar	Salt
99		OH	H		
100		OH	H		HCl
101		OH	H		
102		OH	H		HCl
103		OH	H		HCl
104		OH	H		HCl
105		OH	H		

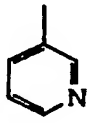
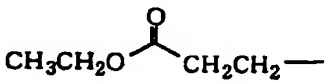
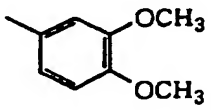
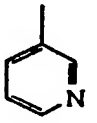
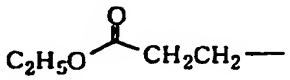
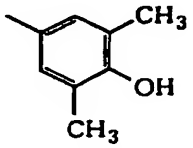
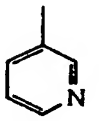
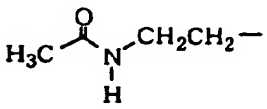
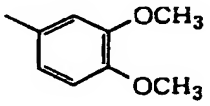
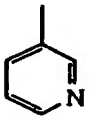
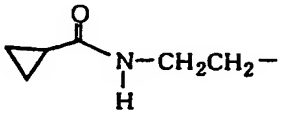
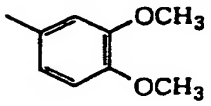
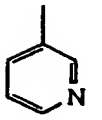
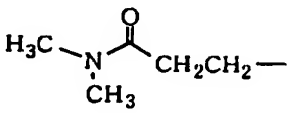
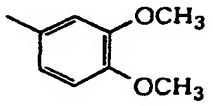
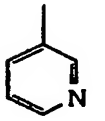
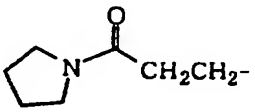
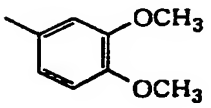
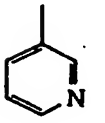
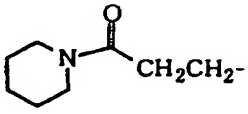
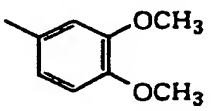
Comp. No.	Q	T	R^1	Ar	Salt
106		OH	H		HCl
107		OH	H		
108		OH	H		HCl
109		CH_3-$(CH_2)_3$—	H		
110		CH_3-$(CH_2)_3$—	H		HCl
111		CH_3-$(CH_2)_3$—	H		HCl
112		CH_3-$(CH_2)_3$—	H		

Comp. No.	Q	T	R^1	Ar	Salt
113			H		
114			H		
115		CH_3-	H		
116		CH_3-	H		HCl
117		CH_3-	H		HCl
118	CH_3-$(CH_2)_7$—		H		
119	CH_3-$(CH_2)_7$—		H		

Comp. No.	Q	T	R^1	Ar	Salt
120	$CH_3-(CH_2)_7-$	CH_3-	H		
121	$CH_3-(CH_2)_7-$	CH_3-	H		
122	$CH_3-(CH_2)_5-$	CH_3-	H		
123	$CH_3-(CH_2)_5-$	CH_3-	H		
124	$CH_3-(CH_2)_2-$	CH_3-	H		
125	$CH_3-(CH_2)_2-$	CH_3-	H		
126			H		HCl

Comp. No.	Q	T	R^1	Ar	Salt
127			H		
128			H		
129			H		
130			H		
131			H		HCl
132			H		HCl
133			H		HCl

Comp. No.	Q	T	R^1	Ar	Salt
134			H		
135			H		
136			H		
137			H		
138		$CH_3OCH_2CH_2$-	H		
139		$CH_3CH_2OCH_2CH_2$-	H		
140			H		

Comp. No.	Q	T	R^1	Ar	Salt
141			H		
142			H		
143			H		
144			H		
145			H		
146			H		
147			H		

EXAMPLE 6.

Preparation of 3-(2-*N*, *N*-dimethylaminoethyl)-2-(3-pyridyl)-5-(4-hydroxy-3-methoxyphenylallyliden)-thiazolidine-4-one hydrochloride salt(Compound No. 148)

A solution of 4-hydroxy-3-methoxy-cinnamaldehyde(2.0 g, 11.2 mmol) in tetrahydrofuran(20 mL) was cooled to 0 ℃ and added 80 % NaH(0.404 g, 13.5 mmol). After stirred for 10 min at 0 ℃, to the reaction mixture was added 2-methoxyethoxymethyl chloride (1.68 g, 13.5 mmol) and warmed to room temperature. After stirred for 3 h, the reaction mixture was cooled to 0 ℃ and added methanol(4 mL). When no more evolution of hydrogen gas the reaction mixture was warmed to room temperature added water(10 mL), and extracted with ethyl acetate(2 x 50 mL). The combined organic phase was dried over anhydrous magnesium sulfate, filtered, and evaporated to dryness. The residue was purified by flash column chromatography on silica gel to give 2.74 g(92 %) of 3-methoxy-4-(2-methoxyethoxymethyloxy)-cinnamaldehyde.

^{1}H NMR(300 MHz, $CDCl_3$) δ : 9.66(d, *J*=7.8Hz, 1H), 7.42(d, *J*=15.9Hz, 1H), 7.24 (d, *J*=8.4Hz, 1H), 7.13(dd, *J*=8.4, 2.1Hz, 1H), 7.09 (d, *J*=2.1Hz, 1H), 6.62(dd, *J*=15.9, 7.8Hz, 1H), 5.38(s, 2H), 3.89(s, 3H), 3.85(m, 2H), 3.55(m, 2H), 3.37(s, 3H)

To a solution of 3-(2-*N*,*N*-dimethylaminoethyl)-2-(3-pyridyl)-thiazolidin-4-one (1.00g, 3.98 mmol) in tetrahydrofuran(30 mL) was added lithium diisopropylamide (1.5M solution, 3.18 mL) at -78 ℃ and stirred for 10 min. To the reaction mixture was slowly added 3-methoxy-4-(2-methoxyethoxymethyloxy)-cinnamaldehyde(1.27 g, 4.77 mmol) dissolved in tetrahydrofuran(5 mL). After stirred at -78 ℃ for 3 h, the reaction mixture was added acetic acid(4 mL) and allowed to warm to room temperature. The reaction mixture was neutralized with saturated sodium bicarbonate solution and extracted with ethyl acetate(2 x 50 mL). The combined organic phase was dried over anhydrous magnesium sulfate, filtered, and evaporated to

dryness. The residue was dissolved in 30% HCl-ethanol solution(10 mL) stirred at room temperature for 3h and then neutralized with saturated sodium bicarbonate solution, extracted with ethyl acetate(2 x 50 mL). The combined organic phase was dried over anhydrous magnesium sulfate, filtered, and evaporated to give pale yellow solids. The residue was purified by flash column chromatography on silica gel to give 1.35 g (83 %) of 3-(2-*N,N*-dimethylaminoethyl)-2-(3-pyridyl)-5-(4-hydroxy-3-methoxyphenylallylidene) thiazolidin-4-one.

^{1}H NMR(300 MHz, $CDCl_3$) δ : 8.62(m, 2H), 7.65(m, 1H), 7.38(m, 1H), 7.23(d, *J*= 11.1Hz, 1H), 6.98(d, *J*=8.4Hz, 1H), 6.92(s, 1H), 6.85(d, *J*=8.4Hz, 1H), 6.75(d, *J*=15.3Hz, 1H), 6.58 (dd, *J*=15.3, 11.1Hz, 1H), 6.15(s, 1H), 3.92(m, 1H), 3.91(s, 3H), 2.83(m, 1H), 2.59(m, 1H), 2.28(m, 1H), 2.20(s, 6H)

To a solution of 3-(2-*N,N*-dimethylaminoethyl)-2-(3-pyridyl)-5-(4-hydroxy-3-methoxyphenylallylidene)thiazolidin-4-one(1.35 g, 3.28 mmol) in ethanol(4 mL) was added 30 % HCl-ethanol solution(0.98 mL) and stirred at room temperature for 1 h. To the reaction mixture was added ethyl acetate(30 mL), filtered, and evaporated to give 1.53 g(97 %) of 3-(2-*N,N*-dimethylaminoethyl)-2-(3-pyridyl)-5-(4-hydroxy-3-methoxyphenylallylidene)-thiazolidine-4-one hydrochloride salt.

EXAMPLE 7.

Preparation of 3-(2-*N,N*-dimethylaminoethyl)-2-(3-pyridyl)-5-(3,5-diemthyl-4-hydroxyphenylallylidene)-thiazolidine-4-one (Compound No. 150)

A solution of 3,5-dimethyl-4-hydroxycinnamaldehyde(2.0 g, 11.4 mmol) in tetrahydrofuran(25 mL) was cooled to 0 ℃ and added 80 % NaH(0.425 g, 14.2 mmol). After stirred for 15 min at 0 ℃, to the reaction mixture was added 2-methoxyethoxymethyl chloride(2.12 g, 17.0 mmol) and warmed to room temperature. After stirred for 4 h, the reaction mixture was cooled to 0 ℃, added methanol(10 mL) and then warmed to room temperature, added water(20 mL), and extracted with ethyl

acetate(2 x 40 mL). The combined organic phase was dried over anhydrous magnesium sulfate, filtered, and evaporated to dryness. The residue was purified by flash column chromatography on silica gel to give 2.34 g(78 %) of 3,5-dimethyl-4-(2-methoxyethoxymethyloxy)-cinnamaldehyde.

^{1}H NMR(300 MHz, $CDCl_3$) δ : 9.65(d, J=7.8Hz, 1H), 7.36(d, J=15.6Hz, 1H), 7.24 (s, 2H), 6.02(dd, J=15.6, 7.8Hz, 1H), 5.09(s, 2H), 3.95(m, 2H), 3.62(m, 2H), 3.40(s, 3H), 2.31(s, 6H)

To a solution of 3-(2-*N*,*N*-dimethylaminoethyl)-2-(3-pyridyl)-thiazolidin-4-one (0.193g, 0.768 mmol) in tetrahydrofuran(8 mL) was added lithium diisopropylamide (1.5M solution, 1.0 mL) at -78 ℃ and stirred for 5 min. To the reaction mixture was slowly added 3,5-dimethyl-4-(2-methoxyethoxymethyloxy)-cinnamaldehyde(0.225 g, 0.683 mmol) dissolved in tetrahydrofuran(1 mL). After stirred at -35 ℃ ~ -40 ℃ for 1 h, the reaction mixture was added acetic acid(1mL), allowed to warm to room temperature, and evaporated. To the residue was added 30 % HCl-ethanol solution(5 mL), stirred at room temperature for 2 h and it was then neutralized with saturated sodium bicarbonate solution and extracted with ethyl acetate(2 x 25 mL). The combined organic phase was dried over anhydrous magnesium sulfate, filtered, and evaporated to dryness. The residue was purified by flash column chromatography on silica gel to give 0.14 g (45 %) of 3-(2-*N*, *N*-dimethylaminoethyl)-2-(3-pyridyl)-5-(3,5-diemthyl-4-hydroxyphenylallylidene)-thiazolidine-4-one.

^{1}H NMR(300 MHz, $CDCl_3$) δ : 8.64~8.59(m, 2H), 7.69~7.66(m, 1H), 7.37~7.33(m, 1H), 7.22(d, J=11.1Hz, 1H), 7.09(s, 2H), 6.72(d, J= 15.3Hz, 1H), 6.55(dd, J=15.3, 11.1Hz, 3.98~3.90 (m, 1H), 2.86~2.77(m, 1H), 2.60~2.51(m, 1H), 2.37~2.28(m, 1H), 2.24(s, 6H), 2.18(s, 6H)

EXAMPLE 8.

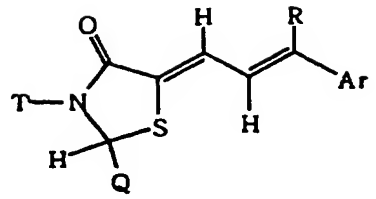
Preparation of 3-(2-*N*,*N*-dimethylaminoethyl)-2-(3-pyridyl)-5-(3,5-diemthyl-4-ethoxycarbonyloxyphenylallylidene)-thiazolidine-4-one (Compound No. 175)

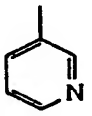
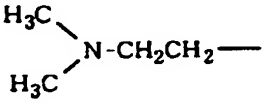
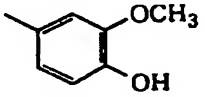
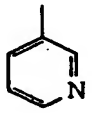
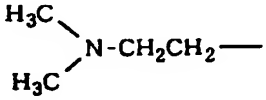
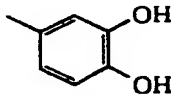
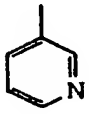
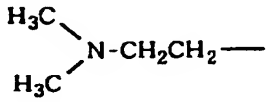
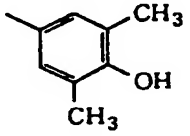
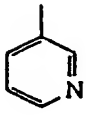
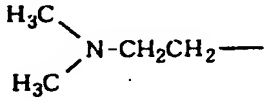
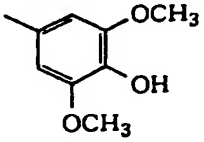
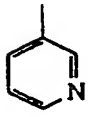
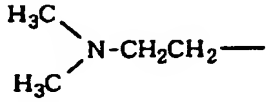
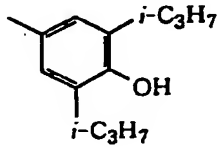
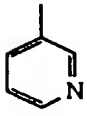
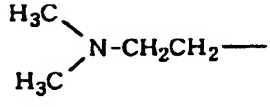
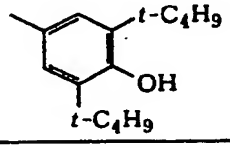
To a solution of 3-(2-*N*,*N*-dimethylaminoethyl)-2-(3-pyridyl)-5-(3,5-diemthyl-4-hydroxyphenylallylidene)-thiazolidine-4-one(0.537 g,1.31 mmol) in pyridine(5 mL) was added ethyl chloroformate(0.284 g, 2.62 mmol), stirred at room temperature for 3 h, and evaporated. The residue was neutralized with saturated sodium bicarbonate solution and extracted with ethyl acetate(4 x 20 mL). The combined organic phase was dried over anhydrous magnesium sulfate, filtered, and evaporated to dryness. The residue was purified by flash column chromatography on silica gel to give 1.35 g (83 %) of3-(2-*N*, *N*-dimethylaminoethyl)-2-(3-pyridyl)-5-(3,5-diemthyl-4-ethoxycarbonyloxyphenylallylidene)-thiazolidine-4-one.

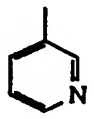
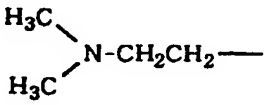
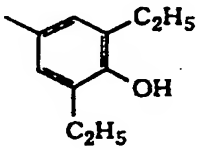
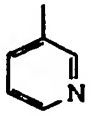
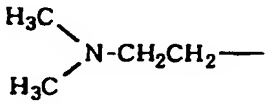
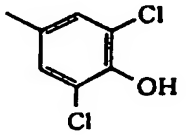
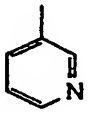
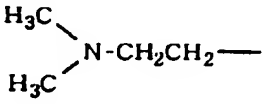
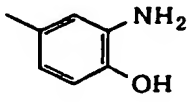
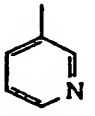
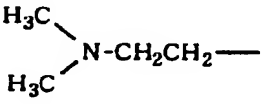
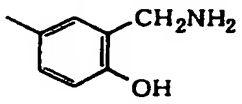
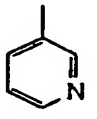
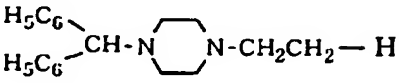
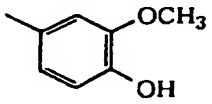
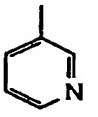
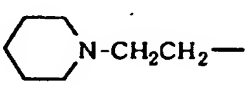
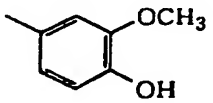
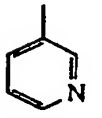
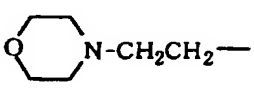
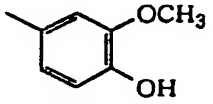
^{1}H NMR(300 MHz, $CDCl_3$) δ : 8.65~8.61(m, 2H), 7.68(m, 1H), 7.35(m, 1H), 7.21 (d, *J*=11.1Hz, 1H), 7.10(s, 2H), 6.72(d, *J*=15.3Hz, 1H), 6.55(dd, *J*=15.3, 11.1Hz, 1H), 3.99(m, 1H), 3.53(q, *J*=7.6Hz, 2H), 2.83(m, 1H), 2.65(m, 1H), 2.30(m, 1H), 2.24(s, 6H), 2.19(s, 6H), 1.25(t, *J*= 7.6Hz, 3H)

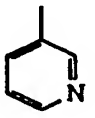
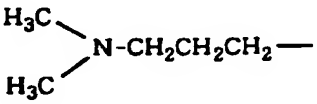
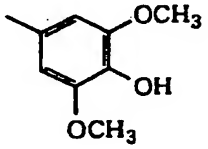
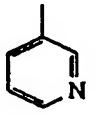
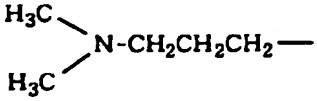
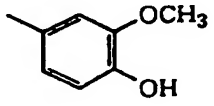
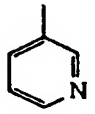
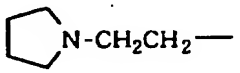
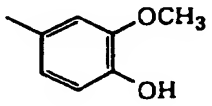
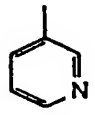
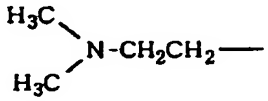
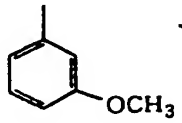
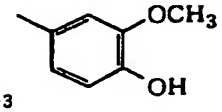
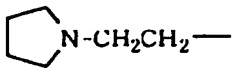
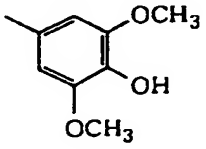
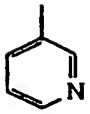
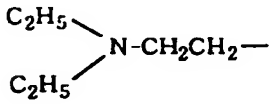
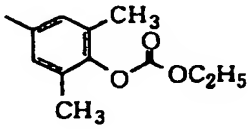
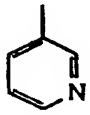
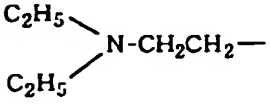
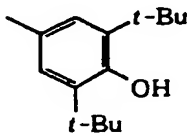
The thiazolidin-4-one derivatives of formula(I) as shown in Table 3, Table 4, and Table 5 were prepared in the same manner as described in EXAMPLE 6 to EXAMPLE 8 using the intermediates of formula(II).

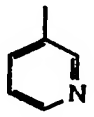
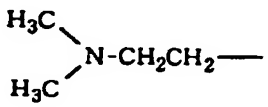
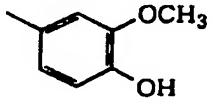
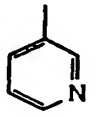
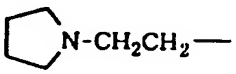
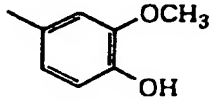
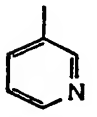
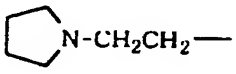
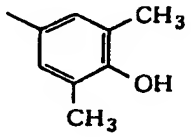
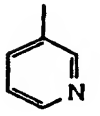
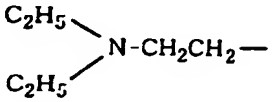
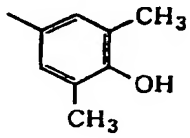
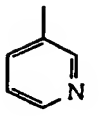
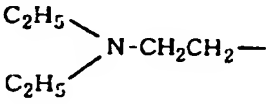
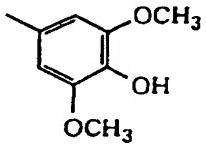
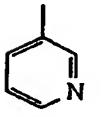
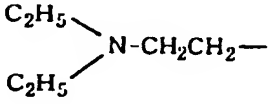
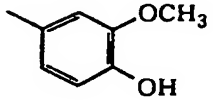
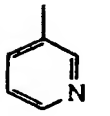
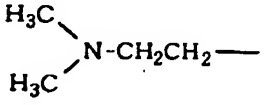
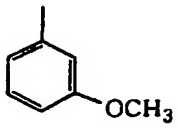
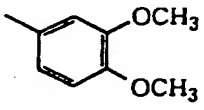
Table 3

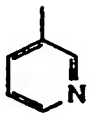
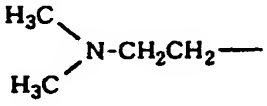
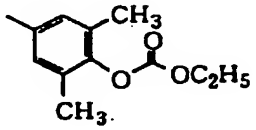
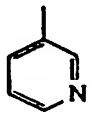
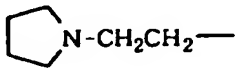
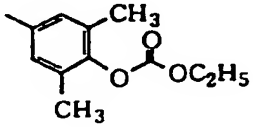
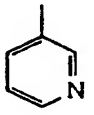
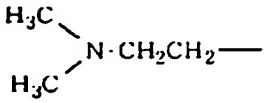
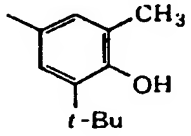
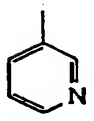
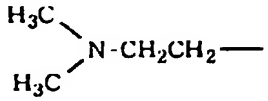
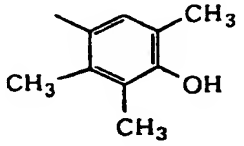
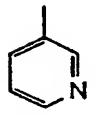
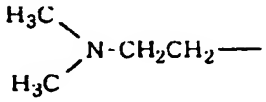
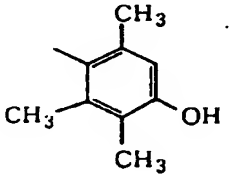
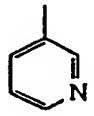
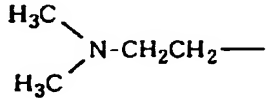
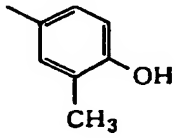
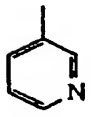
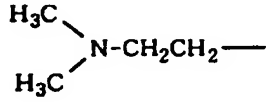
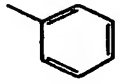


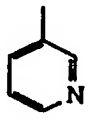
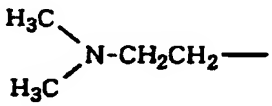
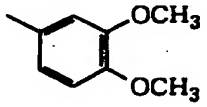
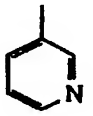
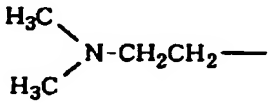
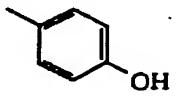
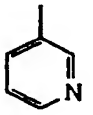
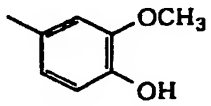
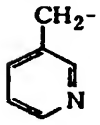
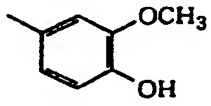
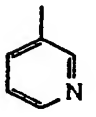
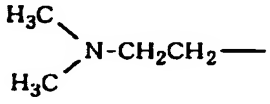
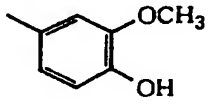
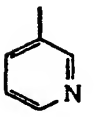
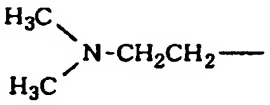
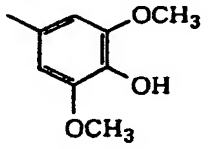
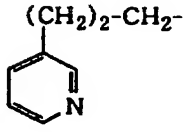
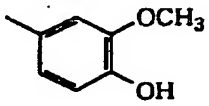
Comp. No.	Q	T	R	Ar	Salt
148			H		
149			H		
150			H		
151			H		
152			H		
153			H		

Comp. No.	Q	T	R	Ar	Salt
154			H		
155			H		
156			H		
157			H		
158			H		
159			H		
160			H		

Comp. No.	Q	T	R	Ar	Salt
161			H		
162			H		
163			CH_3CH_2-		
164					
165			H		
166			H		
167			H		

Comp. No.	Q	T	R	Ar	Salt
168			CH_3CH_2-		
169			H		
170			H		
171			H		
172			H		
173			H		
174					

Comp. No.	Q	T	R	Ar	Salt
175			H		
176			H		
177			H		
178			H		
179			H		
180			H		
181			H		

Comp. No.	Q	T	R	Ar	Salt
182			H		
183			H		
184		CH_3-	H		
185		CH_3-	H		
186			$CH_3CH_2CH_2$-		
187			CH_3CH_2-		
188		CH_3-	H		

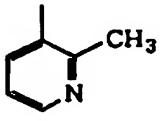
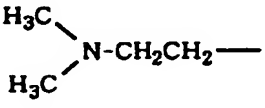
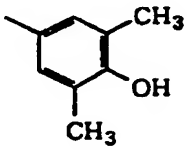
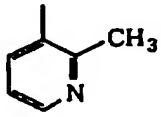
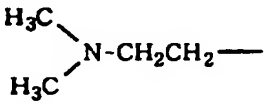
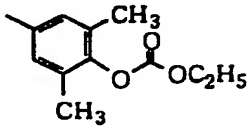
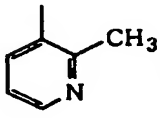
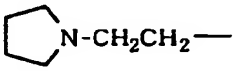
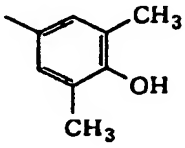
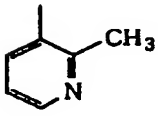
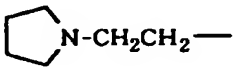
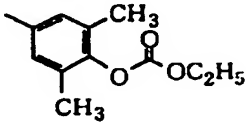
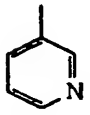
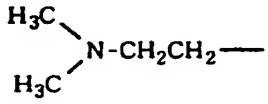
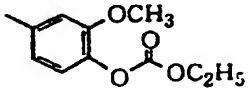
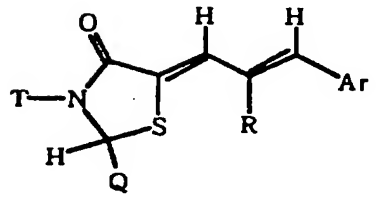
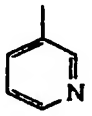
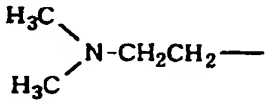
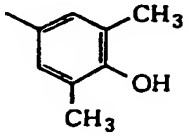
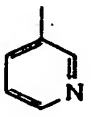
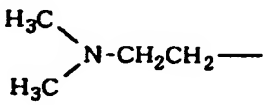
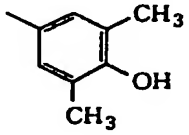
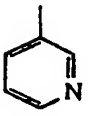
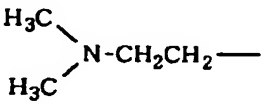
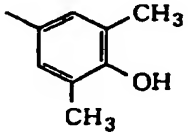
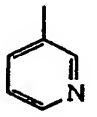
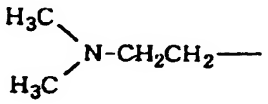
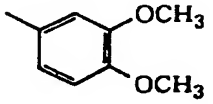
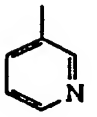
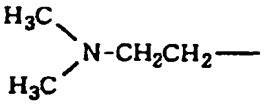
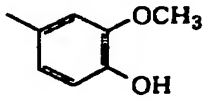
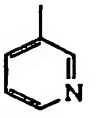
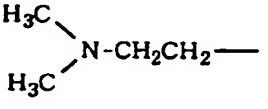
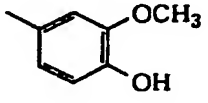
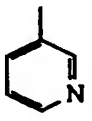
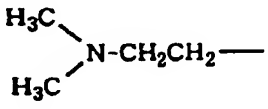
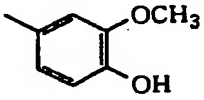
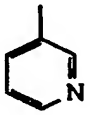
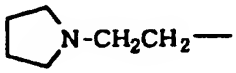
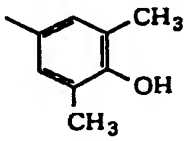
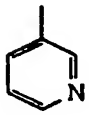
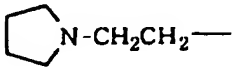
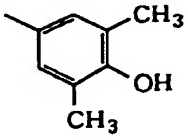
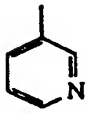
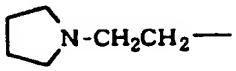
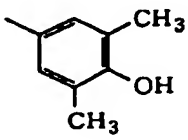
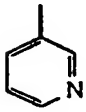
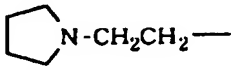
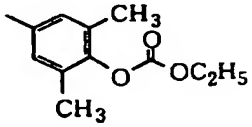
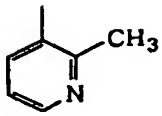
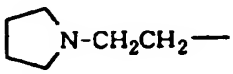
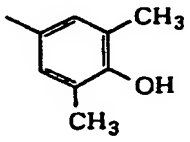
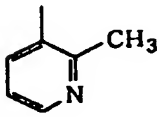
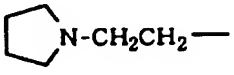
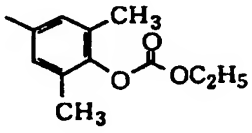
Comp. No.	Q	T	R	Ar	Salt
189			H		
190			H		
191			H		
192			H		
193			H		

Table 4



Comp. No.	Q	T	R	Ar	Salt
194			CH_3-		
195			CH_3CH_2-		
196			$CH_3CH_2CH_2$-		
197			CH_3-		
198			CH_3-		
199			CH_3CH_2-		

Comp. No.	Q	T	R	Ar	Salt
200			$CH_3CH_2CH_2$-		
201			CH_3-		
202			CH_3CH_2-		
203			$CH_3CH_2CH_2$-		
204			CH_3-		
205			CH_3-		
206			CH_3-		

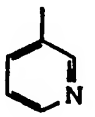
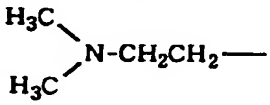
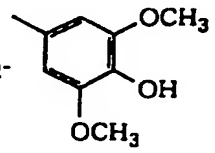
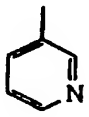
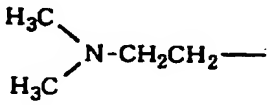
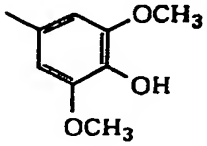
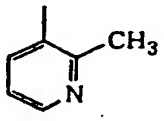
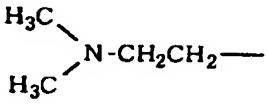
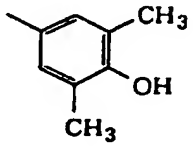
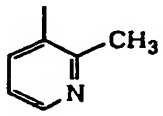
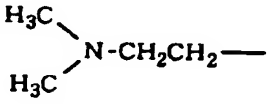
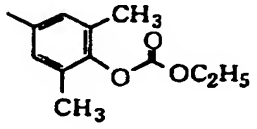
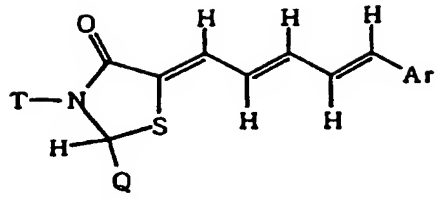
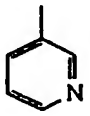
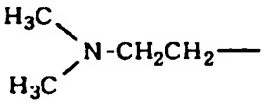
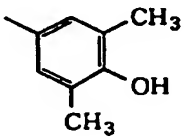
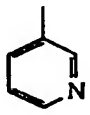
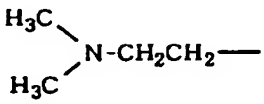
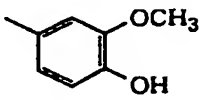
Comp. No.	Q	T	R	Ar	Salt
207			$CH_3CH_2CH_2$-		
208			CH_3CH_2-		
209			CH_3-		
210			CH_3-		

Table 5



Comp. No.	Q	T	Ar
211			
212			

Also NMR datas of the compounds of formula(I) according to the present invention were listed as shown in Table 6.

NMR solvent ; $CDCl_3$

DMSO-d_6(Hydrochloride salts of formula(I))

Table 6

Comp. No.	^{1}H NMR(300 MHz) δ
1	9.70(s, 1H), 8.79(s, 1H), 8.69(d, *J*=4.5Hz, 1H), 7.97(d, *J*=8.1Hz, 1H), 7.60~7.55(m, 6H), 6.39(s, 1H), 4.20~4.12(m, 1H), 3.21~3.00(m, 3H), 2.82(d, *J*=3.9Hz, 6H)
2	8.65(m, 2H), 7.70(m, 1H), 7.50(s, 1H), 7.38(m, 1H), 7.18(d, *J*=8.4Hz, 1H), 7.05(s, 1H), 6.85(d, *J*=8.4Hz, 1H), 6.18(s, 1H), 4.05(m, 1H), 3.90 (s, 3H), 3.89(s, 3H), 2.82(m, 1H), 2.59(m, 1H), 2.38(m, 1H), 2.18(s, 6H)
3	8.63(m, 2H), 7.66(m, 1H), 7.50(s, 1H), 7.36(m, 1H), 6.74(s, 2H), 6.18(s, 1H), 3.98(m, 1H), 3.87(s, 3H), 3.86(s, 3H), 3.85(s, 3H), 2.82(m, 1H), 2.69(m, 1H), 2.38(m, 1H), 2.18(s, 6H)
4	9.70(brs, 1H), 8.74(s, 1H), 8.64(m, 1H), 7.84(m, 1H), 7.80(m, 1H), 7.66 (s, 1H), 7.58(m, 2H), 7.49(m, 1H), 6.38(s, 1H), 4.15(m, 1H), 3.38(m, 1H), 3.00~3.20(m, 2H), 2.82(s, 6H)
6	10.14(brs, 1H), 9.95(s, 1H), 8.79(d, *J*=4.5Hz, 1H), 8.22(d, *J*=8.1Hz, 1H), 7.78(dd, *J*=8.1, 4.5Hz, 1H), 7.31(s, 1H), 6.97(s, 1H), 6.85(s, 2H), 6.46(s, 1H), 4.15(m, 1H), 3.65(m, 1H), 3.40(m, 1H), 3.15(m, 1H), 2.87 (d, *J*=3.6Hz, 6H)
7	8.62(m, 2H), 7.68(m, 1H), 7.50(s, 1H), 7.37(d, *J*=9.0Hz, 2H), 7.35(m, 1H), 6.67(d, *J*=9.0Hz, 2H), 6.11(s, 1H), 3.97(m, 1H), 3.38(q, *J*=7.2Hz, 4H), 2.85(m, 1H), 2.55(m, 1H), 2.14(m, 1H), 2.18(s, 6H), 1.17(t, *J*= 7.2Hz, 6H)
8	8.60(m, 2H), 7.95(s, 1H), 7.70(m, 2H), 7.54(m, 2H), 7.42(m, 1H), 7.38 (m, 1H), 6.17(s, 1H), 4.10(m, 1H), 2.85(m, 1H), 2.60(m, 1H), 2.37(m, 1H), 2.18(s, 6H)

Comp. No.	^{1}H NMR(300 MHz) δ
9	10.02(m, 2H), 8.88(brs, 1H), 8.77(brs, 1H), 8.13(m, 1H), 7.74(s, 2H), 7.15(d, *J*=8.7Hz, 1H), 6.45(s, 1H), 6.39(m, 1H), 6.32(m, 1H), 4.62(brs, 1H), 4.12(m, 1H), 3.40(m, 1H), 3.15(m, 2H), 2.80(s, 6H)
10	9.87(brs, 1H), 8.86(d, *J*=1Hz, 1H), 8.75(d, *J*=4.5Hz, 1H), 8.17(d, *J*= 7.6Hz 1H), 7.75(dd, *J*=7.6, 4.5Hz, 1H), 7.34(s, 1H), 7.12(s, 2H), 6.39(s, 1H), 4.05(m, 1H), 3.15(m, 3H), 2.81(s, 6H), 2.17(s, 6H)
11	8.61(m, 2H), 7.75(m, 1H), 7.54(s, 1H), 7.41(s, 2H), 7.38(m, 1H), 6.15(s, 1H), 4.20(m, 1H), 2.85(m, 1H), 2.62(m, 1H), 2.38(m, 1H), 2.19(s, 6H), 1.43(s, 18H)
12	8.62(m, 2H), 7.68(m, 1H), 7.54(s, 1H), 7.45(d, *J*=9.0Hz, 2H), 7.27(m, 1H), 6.94(d, *J*=9.0Hz, 2H), 6.15(s, 1H), 3.98(m, 1H), 3.83(s, 3H), 2.85 (m, 1H)
13	8.65(m, 1H), 8.61(m, 1H), 7.86(s, 1H), 7.66(m, 1H), 7.43~7.55(m, 2H), 7.30(m, 1H), 7.26(m, 1H), 6.19(s, 1H), 4.01(m, 1H), 2.87(m, 1H), 2.59 (m, 1H), 2.36(m, 1H), 2.19(s, 6H)
14	9.79(brs, 1H), 8.82(s, 1H), 8.72(m, 1H), 8.03(m, 1H), 7.83(s, 1H), 7.65 (m, 1H), 6.83(m, 2H), 6.72(m, 1H), 6.35(s, 1H), 4.14(m, 1H), 3.42(m, 1H), 3.10(m, 2H), 2.82(m, 6H)
15	9.72(brs, 1H), 9.43(brs, 1H), 8.80(brs, 1H), 8.70(brs, 1H), 7.98(m, 1H), 7.75(s, 1H), 7.62(m, 1H), 6.82(m, 1H), 6.75(m, 1H), 6.62(m, 1H), 6.35(s, 1H), 4.15(m, 1H), 3.40(m, 1H), 3.10(m, 2H), 2.82(m, 6H)
16	9.50(brs, 1H), 9.00(brs, 1H), 8.72(m, 1H), 8.66(m, 1H), 7.88(m, 1H), 7.78(s, 1H), 7.50(m, 1H), 6.72(d, *J*=8.7Hz, 1H), 6.40(d, *J*=8.7Hz, 1H), 6.25(s, 1H), 4.12(m, 1H), 3.36(m, 1H), 3.08(m, 2H), 2.80(m, 6H)

Comp. No.	^{1}H NMR(300 MHz) δ
17	8.65(m, 1H), 8.60(m, 1H), 7.66(m, 1H), 7.39~7.49(m, 5H), 7.20~7.39 (m, 7H), 7.09(d, *J*=1.8Hz, 1H), 7.03(m, 1H), 6.94(m, 1H), 6.12(s, 1H), 5.19(s, 2H), 5.17(s, 2H), 3.98(m, 1H), 2.84(m, 1H), 2.54(m, 1H), 2.33(m, 1H), 2.18(s, 6H)
22	10.09(brs, 1H), 8.99(s, 1H), 8.82(d, *J*=4.8Hz, 1H), 8.29(d, *J*=8.1Hz, 1H), 7.83(dd, *J*=7.8, 5.4Hz, 1H), 7.45(s, 1H), 7.38(t, *J*=7.8Hz, 1H), 7.10 (d, *J*=7.8Hz, 1H), 7.06(s, 1H), 6.94(dd, *J*=8.4, 1.8Hz, 1H), 6.52(s, 1H), 4.15(m, 1H), 3.82(s, 3H), 3.04~3.27(m, 2H), 2.81(s, 6H)
23	9.77(brs, 1H), 8.82(m, 1H), 8.74(m, 1H), 8.02(m, 1H), 7.64(m, 1H), 7.43 (s, 1H), 6.82(s, 2H), 6.38(s, 1H), 4.15(m, 1H), 3.93(t, *J*=6.3Hz, 4H), 3.86(t, *J*=6.3Hz, 2H), 2.96~3.37(m, 3H), 2.81(s, 6H), 1.73(m, 4H), 1.65 (m, 2H), 0.98(m, 9H)
38	8.59(m, 2H), 7.62(m, 1H), 7.47(s, 1H), 7.32(m, 1H), 7.16(s, 2H), 6.21(s, 1H), 3.82(m, 1H), 2.85(m, 2H), 2.45(m, 5H), 2.29(s, 6H), 0.95(t, *J*= 6.9Hz, 6H)
39	10.1(brs, 1H), 8.93(s, 1H), 8.81(m, 1H), 8.24(m, 1H), 7.79(m, 1H), 7.31 (s, 1H), 6.96(s, 1H), 6.83(m, 2H), 6.24(s, 1H), 4.04(m, 1H), 3.24(m, 2H), 3.13(m, 4H), 1.17(t, *J*=7.2Hz, 6H)
40	8.62(m, 2H), 7.68(m, 2H), 7.53(s, 1H), 7.35(m, 1H), 7.08(d, *J*=8.2Hz, 1H), 7.05(s, 1H), 6.90(d, *J*=8.2Hz, 1H), 6.19(s, 1H), 4.01(m, 1H), 3.90 (s, 3H), 3.89(s, 3H), 2.80~3.02(m, 2H), 2.48(m, 5H), 1.77(m, 4H)

Comp. No.	^{1}H NMR(300 MHz) δ
47	8.63(m, 2H), 7.67(m, 1H), 7.53(s, 1H), 7.35(m, 1H), 7.08(d, *J*=8.4Hz, 1H), 7.05(s, 1H), 6.90(d, *J*=8.4Hz, 1H), 6.21(s, 1H), 3.95(m, 1H), 3.90 (s, 6H), 2.91(m, 1H), 2.82(m, 1H), 2.35(m, 5H), 1.57(m, 1H), 1.44(m, 2H)
50	8.65(m, 1H), 8.61(m, 1H), 7.71(m, 1H), 7.53(s, 1H), 7.36(m, 1H), 7.09 (d, *J*=8.4Hz, 1H), 7.05(s, 1H), 6.91(d, *J*=8.4Hz, 1H), 6.14(s, 1H), 3.96 (m, 1H), 3.90(s, 3H), 3.89(s, 3H), 3.69(m, 4H), 2.93(m, 1H), 2.61(m, 1H), 2.43(m, 1H), 2.41(m, 4H)
67	8.81(s, 1H), 8.76(d, *J*=4.8Hz, 1H), 8.08(d, *J*=8.1Hz, 1H), 7.73(m, 1H), 7.16~7.29(m, 6H), 6.95(s, 1H), 6.83(s, 2H), 6.22(s, 1H), 3.92(m, 1H), 3.05(m, 1H), 2.95(m, 1H), 2.89(m, 1H)
69	8.60(s, 1H), 8.59(s, 1H), 7.72(d, *J*=7.8Hz, 1H), 7.45(m, 1H), 7.40(s, 1H), 6.99~7.27(m, 8H), 6.03(s, 1H), 3.95(m, 1H), 3.80(s, 3H), 3.79(s, 3H), 2.80~3.05(m, 2H), 2.60~2.80(m, 1H)
71	8.79(s, 1H), 8.75(d, *J*=4.8Hz, 1H), 8.08(d, *J*=8.1Hz, 1H), 7.72(m, 1H), 7.39(s, 1H), 7.27(s, 2H), 7.17(m, 5H), 6.20(s, 1H), 4.05(m, 1H), 3.05(m, 1H), 2.92(m, 1H), 2.85(m, 1H), 1.37(s, 18H)
72	8.62(d, *J*=5.1Hz, 1H), 8.39(s, 1H), 7.61~7.51(m, 2H), 7.40~7.30(m, 1H), 7.07(dd, *J*=8.1, 2.1Hz, 1H), 7.03(d, *J*=2.1Hz, 1H), 6.91(d, *J*=8.1Hz, 1H), 6.83(d, *J*=8.1Hz, 1H), 6.68(dd, *J*=8.1, 1.5Hz, 1H), 6.64(d, *J*= 1.5Hz, 1H), 5.26(s, H), 4.10(m, 1H), 3.90(s, 3H), 3.89(s, 3H), 3.88(s, 3H), 3.82(s, 3H), 3.05~2.70(m, 3H)

Comp. No.	^{1}H NMR(300 MHz) δ
74	8.76(m, 2H), 8.05(m, 1H), 7.71(m, 1H), 7.40(s, 1H), 7.11(s, 1H), 7.05(s, 1H), 6.83(d, J=8.4Hz), 6.73(s, 1H), 6.65(d, J=8.4Hz), 6.15(s, 1H), 4.05 (m, 1H), 3.78(s, 3H), 3.76(s, 3H), 3.05(m, 1H), 2.80(m, 1H), 2.65(m, 1H), 2.17(s, 6H)
78	8.65(d, J=3.9Hz, 1H), 8.50(s, 1H), 7.70(d, J=8.1Hz, 1H), 7.61(s, 1H), 7.40(m, 1H), 7.10(d, J=6.9Hz, 1H), 7.04(s, 1H), 6.89(d, J=8.1Hz, 1H), 6.70(d, J=7.8Hz, 1H), 6.67(s, 1H), 6.52(d, J=7.8Hz), 5.96(s, 2H), 5.61 (s, 1H), 4.44(ABq, $\Delta\nu$ =477, J_{AB}=14.4Hz, 2H), 3.90(s, 3H), 3.89(s, 3H)
79	8.72(m, 2H), 8.06(d, J=6.2Hz, 1H), 7.71(m, 1H), 7.36(s, 1H), 6.95(s, 1H), 6.79(m, 3H), 6.69(s, 1H), 6.58(d, J=7.8Hz, 1H), 6.13(s, 1H), 5.97 (s, 2H), 4.43(ABq, $\Delta\nu$ =228, J_{AB}=15.3Hz, 2H)
80	8.78~8.76(m, 2H), 8.15(d, J=8.1Hz), 7.77(dd, J=8.1, 5.4Hz, 1H), 7.51(s, 1H), 7.30(s, 2H), 6.78(d, J=8.1Hz, 1H), 6.70(s, 1H), 6.58(d, J=8.1Hz, 1H), 6.17(s, 1H), 5.99(s, 2H), 4.45(ABq, $\Delta\nu$ =205.5, J_{AB}=15Hz, 2H), 1.38(s, 18H)
81	8.60(m, 2H), 8.52(m, 1H), 7.71(m, 1H), 7.66(m, 1H), 7.60(s, 1H), 7.46 (d, J=8.7Hz, 2H), 7.35(m, 1H), 7.22(m, 1H), 6.94(d, J=8.7Hz, 2H), 6.04 (s, 1H), 5.21(d, J=15.3Hz, 1H), 4.04(d, J=15.3Hz, 1H), 3.83(s, 3H)
82	8.56~8.67(m, 2H), 8.52(m, 1H), 7.72(m, 1H), 7.65(m, 1H), 7.59(s, 1H), 7.34(m, 1H), 7.27(d, J=6.6Hz, 1H), 7.20(m, 1H), 7.10(m, 1H), 7.06(m, 1H), 6.91(d, J=6.6Hz, 1H), 6.04(s, 1H), 5.22(d, J=15.3Hz, 1H), 4.03(d, J=15.3Hz, 1H), 3.91(s, 3H), 3.90(s, 3H)

Comp. No.	^{1}H NMR(300 MHz) δ
83	8.62(m, 2H), 8.53(m, 2H), 7.73(m, 1H), 7.66(m, 1H), 7.56(s, 1H), 7.35 (m, 1H), 7.21(m, 1H), 6.76(s, 2H), 6.07(s, 1H), 5.22(d, J=15.3Hz, 1H), 4.04(d, J=15.3Hz, 1H). 3.87(s, 9H)
84	8.82(s, 1H). 8.73(m, 1H), 8.55(m, 1H), 8.20(m, 1H), 7.95(m, 1H), 7.74 (m, 1H), 7.43(m, 2H), 7.35(s, 1H), 6.98(m, 1H), 6.85(m, 2H), 6.36(s, 1H), 5.01(d, J=16.2Hz, 1H), 4.36(d, J=16.2Hz, 1H)
85	8.70(m, 2H), 7.90(m, 1H), 7.58(m, 1H), 7.43(s, 1H), 6.85(s, 2H), 6.30(s, 1H), 3.42(m, 11H), 1.42(m, 2H), 0.98(t, J=7.6Hz, 3H)
86	8.62(m, 1H), 8.53(m, 1H), 8.49(m, 1H), 7.61(m, 2H), 7.50(s, 1H), 7.33 (m, 1H), 7.19(m, 2H), 7.07(m, 1H), 7.02(m, 1H), 6.90(m, 1H), 5.65(s, 1H), 4.20(m, 1H), 3.90(s, 3H), 3.89(s, 3H), 3.31(m, 1H), 3.14(m, 1H), 3.06(m, 1H)
87	8.61(m, 1H), 8.44~8.57(m, 2H), 7.60~7.74(m, 2H), 7.51(s, 1H), 7.18~7.37(m, 4H), 7.07(d, J=7.5Hz, 1H), 7.01(s, 1H), 6.90(m, 1H), 5.73 (s, 1H), 4.21(m, 1H), 3.81(s, 3H), 3.30(m, 1H), 3.17(m, 2H)
88	8.62(m, 1H), 8.53(m, 1H), 8.48(m, 1H), 7.56~7.70(m, 2H), 7.51(s, 1H), 7.43(d, J=8.7Hz, 2H), 7.29~7.37(m, 1H), 7.12~7.23(m, 2H), 6.93(d, J= 8.7Hz, 2H), 5.63(s, 1H), 4.21(m, 1H), 3.82(s, 3H), 3.30(m, 1H), 3.15(m, 1H), 3.05(m, 1H)
89	8.72(m, 2H), 8.25(m, 1H), 7.93(m, 1H), 7.74(m, 2H), 7.60(m, H), 7.21(s, 1H), 7.07(s, 2H), 6.33(s, 1H), 4.12(m, 1H), 3.20(m, 3H), 2.16(s, 6H)

Comp. No.	^{1}H NMR(300 MHz) δ
90	8.69(m, 2H), 8.37(s, 1H), 7.78(d, J=7.8Hz, 1H), 7.50(s, 1H). 7.41(m, 1H), 6.74(s, 2H), 5.99(s, 1H), 4.40(m, 1H), 4.13(m, 1H), 3.87(s, 9H), 3.17(d, J=14.4Hz, 1H), 3.05(d, J=14.4Hz, 1H), 2.04(s, 3H)
91	9.90(brs, 1H), 8.89(s, 1H), 8.78(m, 1H), 8.20(d, J=7.6Hz, 1H), 7.79(m, 1H), 7.42(s, 1H), 7.08(m, 3H), 6.35(s, 1H), 3.89(m, 1H), 3.85(m, 1H), 3.78(s, 3H), 3.77(s, 3H), 3.61(m, 1H), 3.00(m, 1H), 1.94(s, 3H)
92	8.68(s, 2H), 8.42(s, 1H). 7.78(d, J=7.6Hz, 1H), 7.52(s, 1H), 7.41(m, 1H), 7.10(d, J=8.4Hz, 1H), 7.03(s, 1H), 6.90(d, J=8.4Hz, 1H), 6.00(s, 1H), 5,20(brs, 2H), 4.08(m, 2H), 3.91(s, 3H), 3.89(s, 3H), 3.14(m, 2H)
93	10.54(s, 1H), 8.83(s, 1H), 8.64(m, 1H), 7.77(d, J=7.8Hz, 1H), 7.48(m, 1H), 7.44(s, 1H), 6.88(s, 2H), 6.24(s, 1H), 3.86(m, 1H), 3.79(s, 6H), 3.69 (s, 3H), 3.02(m, 1H), 2.38(m, 1H), 2.15(m, 1H)
94	8.64(s, 1H), 8.49(d, J=2.4Hz, 1H), 7.74(d, J=7.5Hz, 1H), 7.42(s, 1H), 6.96(d, J=8.4Hz, 1H), 6.93(s, 1H), 6.78(d, J=8.4Hz, 1H), 6.12(s, 1H), 4.38(d, J=15.9Hz, 1H), 3.89(s, 3H), 3.84(s, 3H), 3.54(d, J=15.9Hz, 1H)
95	8.71(s, 1H), 8.50(m, 1H), 8.32(d, J=8.4Hz, 1H), 8.24(s, 1H), 7.72(m, 3H), 7.26(m, 1H), 7.09(m, 4H), 6.92(d, J=8.4Hz, 1H), 3.92(s, 6H)
96	8.70(m, 1H), 8.47(m, 1H), 8.26(m, 2H), 7.69(m, 3H), 7.20(m, 1H), 7.07 (s, 1H), 7.05(m, 1H), 6.79(s, 2H), 3.83(s, 3H), 3.82(s, 3H), 3.78(s, 3H)
97	8.72(m, 1H), 8.43(m, 1H), 8.24(m, 1H), 8.09(m), 7.67(m, 2H), 7.39(d, J=8.4Hz, 2H), 7.20(m, 1H), 7.07(s, 1H), 7.05(m, 1H), 6.71(d, J=8.4Hz, 2H), 6.49(s, 1H), 3.84(s, 3H)

Comp. No.	^{1}H NMR(300 MHz) δ
98	8.53(m, 1H), 8.46(s, 1H), 7.52(m, 3H), 7.17(m, 1H), 7.07(d, *J*=8.1Hz, 1H), 7.02(s, 1H), 6.91(d, *J*=8.1Hz, 1H), 5.62(s, 1H), 4.79(m, 1H), 4.40 (m, 1H), 4.15(m, 1H), 3.92(s, 3H), 3.90(s, 3H), 3.61(s, 3H),
99	8.62(m, 2H), 8.05(s, 1H), 7.82(d, *J*=7.8Hz, 1H), 7.49(s, 1H), 7.38(m, 1H), 7.03(s, 2H), 6.00(s, 1H), 3.90(s, 3H), 3.89(s, 3H), 3.88(s, 3H)
100	9.56(s, 1H), 8.81(s, 1H), 8.71(m, 1H), 8.20(d, *J*=8.1Hz, 1H), 7.74(m, 1H), 7.22(s, 1H), 7.08(s, 2H), 6.26(s, 1H), 2.17(s, 6H)
101	8.65(m, 2H), 8.06(s, 1H), 7.82(m, 1H), 7.50(s, 1H), 7.39(m, 1H), 7.09(d, *J*=8.3Hz, 2H), 6.89(d, *J*=8.3Hz, 2H), 6.01(s, 1H), 3.91(s, 3H)
102	9.97(s, 1H), 8.83(s, 1H), 8.73(d, *J*=5.1Hz, 1H), 8.20(d, *J*=7.8Hz), 7.76 (s, 1H), 7.74(m, 1H), 7.56(s, 3H), 6.36(s, 1H)
103	9.56(s, 1H), 8.81(d, *J*=1.5Hz, 1H), 8.72(d, *J*=4.8Hz), 8.19(d, *J*=8.1Hz, 1H), 7.75(m, 1H), 7.20(s, 1H), 6.93(s, 1H), 6.81(s, 2H), 6.26(s, 1H)
107	DMSO-d_6 ; 9.56(s, 1H), 8.80(d, *J*=1.5Hz, 1H), 8.71(d, *J*=4.2Hz, 1H), 8.15(d, *J*=8.1Hz, 1H), 7.73(dd, *J*=7.8, 5.1Hz, 1H), 7.33(s, 1H), 7.27(s, 2H), 6.25(s, 1H), 4.8(brs, 1H), 1.38(s, 18H)
109	8.65(m, 1H), 8.61(m, 1H), 7.68(m, 1H), 7.53(s, 1H), 7.36(m, 1H), 7.04 (m, 2H), 6.90(m, 1H), 5.82(s, 1H), 4.13(q, *J*=6.9Hz, 2H), 3.89(s, 3H), 3.88(m, 1H), 2.79(m, 1H), 1.52(m, 2H), 1.47(t, *J*=6.9Hz, 3H), 1.28(m, 2H), 0.89(t, *J*=7.5Hz, 3H)
110	8.80(s, 1H), 8.72(m, 1H), 8.06(m, 1H), 7.66(m, 1H), 7.42(s, 1H), 7.01~7.17(m, 3H), 6.33(s, 1H), 3.78(s, 3H), 3.77(s, 3H), 3.68(m, 1H), 2.79(m, 1H), 1.42(m, 2H), 1.20(m, 2H), 0.83(t, *J*=4.5Hz, 3H)

Comp. No.	^{1}H NMR(300 MHz) δ
111	8.83(s, 1H), 8.74(s, 1H), 8.10(brs, 1H), 7.74(brs, 1H), 7.28(s, 1H), 6.95 (s, 1H), 6.81(m, 2H), 6.32(s, 1H), 4.25(brs, 2H), 3.75(m, 1H), 2.78(m, 1H), 1.43(m, 2H), 1.22(m, 2H), 0.85(t, *J*=6.3Hz, 3H)
112	8.63(m, 2H), 7.67(m, 1H), 7.53(s, 1H), 7.38(m, 1H), 7.05(d, *J*=8.4Hz, 1H), 7.04(s, 1H), 6.89(d, *J*=8.4Hz, 1H), 5.82(s, 1H), 4.00(t, *J*=6.9Hz, 2H), 3.92(m, 1H), 3.88(s, 3H), 2.80(m, 1H), 1.88(m, 2H), 1.52(m, 2H), 1.32(m, 2H), 1.01(t, *J*=7.2Hz, 3H), 0.89(t, *J*=7.5Hz, 3H)
115	8.66(d, *J*=3.6Hz, 1H), 8.62(d, *J*=1.5Hz, 1H), 7.68(d, *J*=8.1Hz, 1H), 7.54(s, 1H), 7.37(dd, *J*=8.1, 3.6Hz, 1H), 7.10(dd, *J*=8.4, 1.8Hz, 1H), 7.05(s, 1H), 6.91(d, *J*=8.4Hz, 1H), 5.72(s, 1H), 3.90(s, 6H), 2.91(s, 3H)
116	9.39(s, 1H), 9.18(s, 1H), 8.61~8.60(m, 2H), 7.74(d, *J*=8.1Hz, 1H), 7.47 (dd, *J*=8.1, 4.8Hz, 1H), 7.27(s, 1H), 6.97(d, *J*=1.5Hz), 6.85(dd, *J*=8.4, 1.5Hz, 1H), 6.80(d, *J*=8.4Hz, 1H), 6.12(s, 1H), 3.34(s, 2H), 2.80(s, 3H)
117	8.92(d, *J*=1.2Hz, 1H), 8.44(d, *J*=4.8Hz, 1H), 8.28(d, *J*=8.1Hz, 1H), 7.89(dd, *J*=8.1, 4.8Hz, 1H), 7.49(s, 1H), 7.11(d, *J*=1.8Hz, 1H), 6.98(dd, *J*=8.4, 1.8Hz, 1H), 6.88(d, *J*=8.4Hz, 1H), 6.28(s, 1H), 5.40(brs, 3H), 3.78(s, 3H), 2.84(s, 3H)
118	7.26(s, 1H), 6.99(s, 1H), 6.87(d, *J*=8.4Hz, 1H), 6.78(d, *J*=8.4Hz, 1H), 4.96(d, *J*=6.3Hz, 1H), 4.1(brs, 2H, 2OH), 3.25(m, 1H), 2.66(m, 2H), 2.39(s, 6H), 1.87~2.05(m, 1H), 1.56~1.79(m, 1H), 1.31~1.50(m, 12H), 0.87(t, *J*=6.6Hz, 3H)

Comp. No.	^{1}H NMR(300 MHz) δ
119	7.42(s, 1H), 7.14(d, J=8.4Hz, 1H), 7.09(s, 1H), 6.92(d, J=8.4Hz, 1H), 5.05(dd, J=8.1, 2.1Hz, 1H), 3.98(m, 1H), 3.93(s, 3H), 3.91(s, 3H), 3.30 (m, 1H), 2.50(m, 1H), 2.29(s, 6H), 1.92(m, 1H), 1.74(m, 1H), 1.14~1.53 (m, 12H), 0.88(t, J=6.3Hz, 3H)
120	7.36(s, 1H), 7.12(d, J=1.8Hz, 1H), 6.98(d, J=1.8Hz, 1H), 6.91(d, J= 8.1Hz, 1H), 4.77(dd, J=8.4, 1.8Hz, 1H), 3.06(s, 3H). 1.95~2.13(m, 1H), 1.65~1.82(m, 1H), 1.13~1.48(m, 12H), 0.88(t, J=6.6Hz, 3H)
121	7.43(s, 1H), 7.14(dd, J=8.4, 1.5Hz, 1H), 7.09(d, J=1.5Hz, 1H), 6.92(d, J=8.4Hz, 1H), 4.80(dd, J=8.1, 1.8Hz, 1H), 3.93(s, 3H), 3.91(s, 3H), 3.07 (s, 3H), 1.97~2.13(m, 1H), 1.66~1.83(m, 1H), 1.15~1.52(m, 12H), 0.88 (t, J=6.6Hz, 3H)
122	7.36(s, 1H), 7.12(d, J=1.8Hz, 1H), 7.98(dd, J=8.4, 1.8Hz, 1H), 6.91(d, J=8.4Hz), 4.77(dd, J=8.4, 2.7Hz, 1H), 3.06(s, 3H), 1.91~2.12(m, 1H), 1.63~1.81(m, 1H), 1.09~1.52(m, 8H), 0.88(t, J=6.6Hz, 3H)
123	7.43(s, 1H), 7.14(dd, J=8.4, 1,8Hz, 1H), 7.09(d, J=1.8Hz, 1H), 6.94(d, J=8.4Hz, 1H), 4.80(m, 1H), 3.93(s, 3H), 3.91(s, 3H), 3.07(s, 3H), 2.05 (m, 1H), 1.72(m, 1H), 1.30(m, 8H), 0.89(t, J=6.6Hz, 3H)
124	8.03(brs, 2H), 7.33(s, 1H), 7.09(d, J=1.8Hz, 1H), 6.96(dd, J=8.4, 1.8Hz, 1H), 6.89(d, J=8.4Hz, 1H), 4.79(dd, J=8.1, 2.7Hz, 1H), 3.06(s, 3H), 1.95~2.12(m, 1H), 1.65~1.82(m, 1H), 1.32~1.55(m, 2H), 0.98(t, J= 7.2Hz, 3H)

Comp. No.	^{1}H NMR(300 MHz) δ
125	7.43(s, 1H), 7.14(dd, J=8.4, 1.8Hz, 1H), 7.09(d, J=1.8Hz, 1H), 6.92(d, J=8.4Hz, 1H), 4.80(dd, J=8.1, 2.7Hz, 1H), 3.93(s, 3H), 3.91(s, 3H), 3.07 (s, 3H), 1.83~2.11(m, 1H), 1.64~1.84(m, 1H), 1.34~1.55(m, 2H), 0.99(t, J=7.2Hz, 3H)
126	8.59(s, 1H), 8.02(brs, 1H), 7.31~7.52(m, 10H), 6.19(s, 1H), 4.63(ABq, $\Delta\nu$ =224, J_{AB}=16.2Hz, 2H), 1.38(s, 18H)
130	7.51(s, 1H), 7.12(d, J=8.4Hz, 1H), 7.06(s, 1H), 6.91(d, J=8.4Hz, 1H), 6.55(s, 2H), 6.01(s, 1H), 4.01(m, 1H), 3.90(s, 6H), 3.85(s, 9H), 3.00(m, 1H), 2.58(m, 1H), 2.47(m, 1H), 2.26(s, 6H)
131	9.42(s, 1H), 9.21(s, 1H), 7.27(s, 1H), 6.97(s, 1H), 6.84(m, 2H), 6.76(s, 2H), 6.12(s, 1H), 4.12(m, 1H), 3.78(s, 6H), 3.67(s, 3H), 3.26(m, 3H), 2.81(s, 6H)
132	12.37(brs, 1H), 7.43(s, 1H), 7.16(s, 2H), 6.70(s, 2H), 6.10(s, 1H), 4.00 (m, 1H), 3.87(s, 6H), 3.85(s, 3H), 3.68(m, 1H), 3.08~3.13(m, 2H), 2.87 (d, J=4.2Hz, 3H), 2.79(d, J=3.9Hz, 3H), 2.26(s, 6H)
133	10.0(s, 1H), 9.76(s, 1H), 9.41(brs, 1H), 7.71(s, 1H), 7.18(d, J=8.7Hz, 1H), 6.75(s, 2H), 6.40(s, 1H), 6.30(d, J=8.7Hz, 1H), 6.07(s, 1H), 4.05 (m, 1H), 3.78(s, 6H), 2.25(s, 6H)
138	8.63(m, 2H), 7.69(d, J=7.8Hz, 1H), 7.54(s, 1H), 7.35(m, 1H), 7.03~7.16 (m, 2H), 6.91(d, J=8.4Hz, 1H), 6.12(s, 1H), 4.03(m, 1H), 3.91(s, 3H), 3.90(s, 3H), 3.62(m, 1H), 3.52(m, 1H), 3.32(s, 3H), 2.94(m, 1H)

Comp. No.	^{1}H NMR(300 MHz) δ
139	8.62(m, 2H), 7.69(d, J=8.1Hz, 1H), 7.54(s, 1H), 7.35(m, 1H), 7.03~7.16 (m, 2H), 6.91(d, J=8.4Hz, 1H), 6.17(s, 1H), 4.05(m, 1H), 3.91(s, 3H), 3.90(s, 3H), 3.67(m, 1H), 3.40~3.58(m, 3H), 2.93(m, 1H), 1.92(t, J= 7.2Hz, 3H)
140	8.65(m, 2H), 7.68(d, J=8.1Hz, 1H), 7.54(s, 1H), 7.37(m, 1H), 7.09(d, J= 8.4Hz, 1H), 7.04(s, 1H), 6.90(d, J=8.4Hz, 1H), 5.96(s, 1H), 4.30(m, 1H), 4.17(m, 2H), 3.91(s, 3H), 3.90(s, 3H), 3.05(m, 1H), 2.05(s, 3H)
141	8.66(brs, 2H), 7.69(m, 1H), 7.52(s, 1H), 7.36(m, 1H), 7.08(dd, J=8.4, 1.8Hz, 1H), 7.04(d, J=1.8Hz, 1H), 6.90(d, J=8.4Hz, 1H), 6.05(s, 1H), 4.14(q, J=7.2Hz, 2H), 3.91(m, 1H), 3.90(s, 3H), 3.89(s, 3H), 3.19(m, 1H), 2.82(m, 1H), 2.50(m, 1H), 1.25(t, J=7.2Hz, 3H)
145	8.71(m, 1H), 8.61(m, 1H), 7.73(m, 1H), 7.50(s, 1H), 7.33(m, 1H), 7.09 (d, J=8.4Hz, 1H), 7.05(s, 1H), 6.90(d, J=8.4Hz, 1H), 6.27(s, 1H), 3.90 (s, 3H), 3.89(s, 3H), 3.78(m, 1H), 3.35(m, 1H), 3.00(m, 1H), 2.97(s, 3H), 2.94(s, 3H), 2.50(m, 1H)
146	DMSO-d_6; 8.64(m, 1H), 8.60(m, 1H), 7.75(m, 1H), 7.44(m, 1H), 7.41(s, 1H), 7.12~7.05(m, 3H), 6.32(s, 1H), 3.78(s, 3H), 3.77(s, 3H), 3.30~3.21 (m, 5H), 3.05(m, 1H), 2.67(m, 1H), 2.39(m, 1H), 1.77(m, 4H)
148	8.62(m, 2H), 7.65(m, 1H), 7.38(m, 1H), 7.23(d, J=11.1Hz, 1H), 6.98(d, J=8.4Hz, 1H), 6.92(s, 1H), 6.85(d, J=8.4Hz, 1H), 6.75(d, J=15.3Hz, 1H), 6.58(dd, J=15.3, 11.1Hz, 1H), 6.15(s, 1H), 3.92(m, 1H), 3.91(s, 3H), 2.83(m, 1H), 2.59(m, 1H), 2.28(m, 1H), 2.20(s, 6H)

Comp. No.	^{1}H NMR(300 MHz) δ
149	8.60(m, 2H), 7.70(d, J=7.6Hz, 1H), 7.67(s, 1H), 7.39(dd, J=7.6, 4.2Hz, 1H), 7.14(d, J=11.1Hz, 1H), 6.97(s, 1H), 6.78(s, 2H), 6.70(d, J=15.3Hz, 1H), 6.48(dd, J=15.3, 11.1Hz, 1H), 6.17(s, 1H), 3.90(m, 1H), 2.80(m, 1H), 2.50(m, 1H), 2.35(m, 1H), 2.17(s, 6H)
150	8.64~8.59(m, 2H), 7.69~7.66(m, 1H), 7.37~7.33(m, 1H), 7.22(d, J=11.1Hz, 1H), 7.09(s, 2H), 6.72(d, J=15.3Hz, 1H), 6.55(dd, J=15.3, 11.1Hz, 1H), 3.98~3.90(m, 1H), 2.86~2.77(m, 1H), 2.60~2.51(m, 1H), 2.37~2.28(m, 1H), 2.24(s, 6H), 2.18(s, 6H)
151	8.63(m, 2H), 7.67(m, 1H), 7.36(m, 1H), 7.23(d, J=11.1Hz, 1H), 6.75(d, J=15.6Hz, 1H), 6.68(s, 2H), 6.59(dd, J=15.6, 11.2Hz, 1H), 6.16(s, 1H), 3.97(m, 1H), 3.91(s, 6H), 2.84(m, 1H), 2.55(m, 1H), 2.35(m, 1H), 2.18(s, 6H)
152	8.62(m, 2H), 7.69(m, 1H), 7.41(m, 1H), 7.23(s, 2H), 7.08(d, J=11.2Hz, 1H), 6.91(d, J=15.2Hz, 1H), 6.53(dd, J=15.2, 11.2Hz, 1H), 6.24(s, 1H), 5.37(s, 1H), 3.94(m, 1H), 2.82(m, 1H), 2.57(m, 1H), 3.31(m, 2H), 2.31 (m, 1H), 2.18(s, 6H), 1.21(d, J=7.2Hz, 12H)
153	8.61(m, 2H), 7.69(dt, J=7.8, 1.8Hz, 1H), 7.38(m, 1H), 7.25(s, 2H), 7.09 (d, J=11.1Hz, 1H), 6.92(d, J=15Hz, 1H), 6.54(dd, J=15.0, 11.1Hz, 1H), 6.25(s, 1H), 5.37(s, 1H), 3.92(m, 1H), 2.82(m, 1H), 2.56(m, 1H), 2.31(m, 1H), 2.18(s, 6H), 1.45(s, 18H)

Comp. No.	^{1}H NMR(300 MHz) δ
158	8.62(m, 2H), 7.65(m, 1H), 7.38(m, 1H), 7.23(d, *J*=11.1Hz, 1H), 7.11(m, 10H), 6.98(d, *J*=8.4Hz, 1H), 6.92(s, 1H), 6.85(d, *J*=8.4Hz, 1H), 6.75(d, *J*=15.2Hz, 1H), 6.58(dd, *J*=15.2, 11.1Hz, 1H), 6.25(s, 1H), 4.25(s, 1H), 3.92(m, 1H), 3.91(s, 3H), 2.83(m, 3H), 2.65(m, 8H)
159	8.62(m, 2H), 7.58(m, 1H), 7.42(m, 1H), 7.24(d, *J*=11.2Hz, 1H), 6.97(d, *J*=8.4Hz, 1H), 6.91(s, 1H), 6.82(d, *J*=8.4Hz, 1H), 6.72(d, *J*=15.3Hz, 1H), 6.55(dd, *J*=15.3, 11.2Hz, 1H), 6.20(s, 1H), 3.95(m, 1H), 3.92(s, 3H), 2.83(m, 1H), 2.59(m, 6H), 1.82(m, 4H), 0.98(m, 2H)
160	8.64(m, 2H), 7.62(m, 1H), 7.40(m, 1H), 7.24(d, *J*=11.1Hz, 1H), 6.98(d, *J*=8.4Hz, 1H), 6.92(s, H), 6.85(d, *J*=8.4Hz, 1H), 6.76(d, *J*=15.3Hz, 1H), 6.57(dd, *J*=15.3, 11.1Hz, 1H), 6.15(s, 1H), 3.95(m, 5H), 3.91(s, 3H), 3.62(m, 5H), 2.83(m, 1H), 2.59(m, 1H)
161	8.61(m, 2H), 7.68(m, 1H), 7.34(m, 1H), 7.22(d, *J*=11.1Hz, 1H), 6.71(d, *J*=15.6Hz, 1H), 6.68(s, 2H), 6.57(dd, *J*=15.6, 11.1Hz, 1H), 5.93(s, 1H), 3.92(s, 6H), 3.82(m, 1H), 2.86(m, 1H), 2.20~2.40(m, 2H), 2.24(s, 6H), 1.50~1.90(m, 2H)
162	8.63(m, 2H), 7.69(m, 1H), 7.35(m, 1H), 7.23(d, *J*=11.2Hz, 1H), 6.98(d, *J*=8.2Hz, 1H), 6.93(s, 1H), 6.87(d, *J*=8.2Hz, 1H), 6.73(d, *J*=15.6Hz, 1H), 6.57(dd, *J*=15.6, 11.2Hz, 1H), 5.90(s, 1H), 3.92(s, 3H), 3.79(m, 1H), 2.88(m, 1H), 2.26(m, 2H), 2.20(s, 6H), 1.55~1.95(m, 2H)

Comp. No.	^{1}H NMR(300 MHz) δ
163	8.62(m, 2H), 7.65(m, 1H), 7.45(d, *J*=12.0Hz, 1H), 7.33(m, 1H), 6.98(d, *J*=8.4Hz, 1H), 6.85(d, *J*=8.4Hz, 1H), 6.73(s, 1H), 6.18(d, *J*=12Hz, 1H), 6.12(s, 1H), 4.15(m, 1H), 3.89(s, 3H), 2.79(m, 5H), 2.51(m, 4H), 1.74(m, 4H), 1.07(t, *J*=7.6Hz, 3H)
164	8.64(m, 2H), 7.75(m, 1H), 7.33(m, 1H), 7.25(m, 2H), 6.92(t, *J*=8.4Hz, 1H), 6.82(m, 4H), 6.49(t, 1H), 6.12(s, 1H), 3.89(m, 1H), 3.79(s, 3H), 3.76(s, 3H), 2.82(m, 1H), 2.52(m, 1H), 2.31(m, 1H), 2.16(s, 6H)
165	8.63(m, 1H), 8.59(m, 1H), 7.66(m, 1H), 7.36(m, 1H), 7.23(d, *J*= 11.1Hz, 1H), 6.75(d, *J*=15.3Hz, 1H), 6.67(s, 2H), 6.56(dd, *J*=15.3, 11.1 Hz, 1H), 6.17(s, 1H), 3.98(m, 1H), 3.91(s, 6H), 2.84(m, 2H), 2.45(m, 5H), 1.76(m, 4H)
166	8.64(m, 1H), 8.59(m, 1H), 7.66(m, 1H), 7.37(m, 1H), 7.22(d, *J*=10.5Hz, 1H), 7.14(s, 2H), 6.60~6.80(m, 2H), 6.22(s, 1H), 4.32(q, *J*=7.2Hz, 2H), 3.85(m, 1H), 2.68~2.92(m, 2H), 2.16~2.63(m, 5H), 2.20(s, 6H), 1.38(t, *J*=7.2Hz, 3H), 0.99(t, *J*=7.2Hz, 6H)
168	8.61(m, 2H), 7.66(m, 1H), 7.45(d, *J*=12H, 1H), 7.34(m, 1H), 6.98(d, *J*= 8.4Hz, 1H), 6.89(d, *J*=8.4Hz, 1H), 6.73(s, 1H), 6.19(d, *J*=12Hz, 1H), 6.13(s, 1H), 3.90(s, 3H), 3.89(m, 1H), 2.76(m, 3H), 2.57(m, 1H), 2.21(m, 1H), 2.18(s, 6H), 1.22(t, *J*=7.6Hz, 3H)
169	8.63(m, 1H), 8.57(m, 1H), 7.64(m, 1H), 7.38(m, 1H), 7.19(d, *J*=11.4Hz, 1H), 6.95(d, *J*=8.4Hz, 1H), 6.91(s, 1H), 6.83(d, *J*=8.4Hz, 1H), 6.73(d, *J*=15.3Hz, 1H), 6.52(dd, *J*=15.3, 11.4Hz, 1H), 6.15(s, 1H), 4.05(m, 1H), 3.90(s, 3H), 2.82(m, 2H), 2.45(m, 5H), 1.76(m, 4H)

Comp. No.	^{1}H NMR(300 MHz) δ
170	8.63(m, 1H), 8.60(m, 1H), 7.68(m, 1H), 7.37(m, 1H), 7.23(d, *J*=11.1Hz, 1H), 7.08(s, 2H), 6.72(d, *J*=15.3Hz, 1H), 6.56(dd, *J*=15.3, 11.1Hz, 1H), 6.14(s, 1H), 3.96(m, 1H), 2.83(m, 2H), 2.44(m, 4H), 2.24(s, 6H), 1.75(m, 4H)
171	8.63(m, 1H), 8.59(m, 1H), 7.66(m, 1H), 7.35(m, 1H), 7.22(d, *J*=10.8Hz, 1H), 7.09(s, 2H), 6.72(d, *J*=15.2Hz, 1H), 6.58(dd, *J*=15.2, 10.8Hz, 1H), 6.20(s, 1H), 3.84(m, 1H), 2.68~2.92(m, 2H), 2.33~2.60(m, 6H), 2.24(s, 6H), 0.99(t, *J*=7.2Hz, 6H)
173	8.64(m, 1H), 8.59(m, 1H), 7.66(m, 1H), 7.36(m, 1H), 7.21(d, *J*=11.2Hz, 1H), 6.93(d, *J*=8.2Hz, 1H), 6.93(s, 1H), 6.86(d, *J*=8.2Hz, 1H), 6.75(d, *J*=15.2Hz, 1H), 6.57(dd, *J*=15.2, 11.2Hz, 1H), 6.22(s, 1H), 3.91(s, 3H), 3.85(m, 1H), 2.82(m, 2H), 2.52(m, 5H), 0.99(t, *J*=7.2Hz, 6H)
175	8.65~8.61(m, 2H), 7.68(m, 1H), 7.35(m, 1H), 7.21(d, *J*=11.1Hz, 1H), 7.10(s, 2H), 6.72(d, *J*=15.3Hz, 1H), 6.55(dd, *J*=15.3, 11.1Hz, 1H), 3.99 (m, 1H), 6.21(s, 1H), 4.32(q, *J*=7.6Hz, 2H), 2.83(m, 1H), 2.65(m, 1H), 2.30(m, 1H), 2.24(s, 6H), 2.19(s, 6H), 1.25(t, *J*=7.6Hz, 3H)
176	8.64(m, 1H), 8.61(m, 1H), 7.65(m, 1H), 7.36(m, 1H), 7.22(d, *J*=10.5Hz, 1H), 7.14(s, 1H), 6.75(d, *J*=14.3Hz, 1H), 6.64(dd, *J*=14.3, 10.5Hz, 1H), 6.16(s, 1H), 4.32(q, *J*=6.9Hz, 2H), 3.99(m, 1H), 2.83(m, 2H), 2.43(m, 5H), 2.19(s, 6H), 1.75(m, 4H), 1.38(t, *J*=6.9Hz, 3H)

Comp. No.	^{1}H NMR(300 MHz) δ
177	8.64~8.59(m, 2H), 7.70(m, 1H), 7.35(m, 1H), 7.23(d, *J*=14.7Hz, 1H), 7.21(s, 1H), 7.14(s, 1H), 6.77(d, *J*=16.5Hz, 1H), 6.51(dd, *J*=16.5, 14.7Hz, 1H), 6.13(s, 1H), 3.94(m, 1H), 2.82(m, 1H), 2.55(m, 1H), 2.33 (m, 1H), 2.48(s, 3H), 2.18(s, 6H), 1.41(s, 9H)
178	8.61(m, 2H), 7.67(m, 1H), 7.34(m, 1H), 7.27(d, *J*=10.8Hz, 1H), 7.18(s, 1H), 7.10(d, *J*=15Hz, 1H), 6.48(dd, *J*=15, 10.8Hz, 1H), 6.14(s, 1H), 3.95(m, 1H), 2.82(m, 1H), 2.58(m, 1H), 2.40(m, 1H), 2.26(s, 3H), 2.22 (s, 3H), 2.21(s, 3H), 2.18(s, 6H)
179	8.64(m, 1H), 8.58(m, 1H), 7.68(m, 1H), 7.36(m, 1H), 7.27(d, *J*=11.2Hz, 1H), 6.89(d, *J*=15.6Hz, 1H), 6.50(s, 1H), 6.17(dd, *J*=15.6, 11.2Hz, 1H), 6.12(s, 1H), 3.95(m, 1H), 2.80(m, 1H), 2.50(m, 1H), 2.30(m, 1H), 2.24(s, 3H), 2.28(s, 3H), 2.18(s, 6H), 2.15(s, 3H)
180	8.53~8.47(m, 2H), 7.64~7.73(m, 1H), 7.36(dd, *J*=7.8, 4.8Hz, 1H), 7.21 (s, 1H), 7.02~7.12(m, 2H), 6.64~6.71(m, 1H), 6.63(s, 1H), 6.40(dd, *J*= 15.3, 11.1Hz, 1H), 6.11(s, 1H), 3.96~4.08(m, 1H), 2.72~2.87(m, 1H), 2.49~2.60(m, 1H), 2.36~2.49(m, 1H), 2.25(s, 9H)
181	8.65(m, 1H), 8.60(m, 1H), 7.68(m, 1H), 7.44(m, 2H), 7.22~7.41(m, 4H), 6.65~6.92(m, 2H), 6.16(s, 1H), 3.94(m, 1H), 2.82(m, 1H), 2.53(m, 1H), 2.32(m, 1H), 2.17(s, 6H)
182	8.60~8.65(m, 2H), 7.67~7.69(m, 1H), 7.35~7.41(m, 1H), 7.24(d, *J*= 11.4Hz, 1H), 7.00(d, *J*=8.1Hz), 6.82(d, *J*=8.1Hz, 1H), 6.78(d, *J*= 15.1Hz), 6.59(dd, *J*=15.1, 11.4Hz, 1H), 6.15(s, 1H), 3.93(m, 1H), 3.91(s, 3H), 3.90(s, 3H), 2.84(m, 1H), 2.58(m, 1H), 2.33(m, 1H), 2.20(s, 6H)

Comp. No.	^{1}H NMR(300 MHz) δ
183	9.10(brs, 1H), 8.62(m, 2H), 7.67(m, 1H), 7.38(m, 1H), 7.30(d, *J*=8.4Hz, 2H), 7.19(d, *J*=11.2Hz, 1H), 6.81(d, *J*=8.4Hz, 2H), 6.76(d, *J*=15.0Hz, 1H), 6.53(dd, *J*=15.0, 11.2Hz, 1H), 6.15(s, 1H), 3.91(m, 1H), 2.83(m, 1H), 2.54(m, 1H), 2.32(m, 1H), 2.18(s, 6H)
184	8.65(dd, *J*=4.8, 1.5Hz, 1H), 8.60(d, *J*=2.1Hz, 1H), 7.68(td, *J*=7.8, 1.8Hz, 1H), 7.40(m, 1H), 7.24(d, *J*=11.4Hz, 1H), 7.01(dd, *J*=8.1, 1.5Hz, 1H), 6.93(d, *J*=1.5Hz, 1H), 6.88(d, *J*=8.1Hz, 1H), 6.78(d, *J*=15.3Hz, 1H), 6.55(dd, *J*=15.3, 11.4Hz, 1H), 5.70(s, 1H), 3.92(s, 3H), 2.87(s, 3H)
185	8.55(m, 2H), 7.60(m, 1H), 7.29(m, 1H), 7.10(d, *J*=11.4Hz, 1H), 6.97(m, 2H), 6.93(m, 1H), 6.87(d, *J*=8.4Hz, 1H), 6.71(d, *J*=15.3Hz, 1H), 6.51 (dd, *J*=15.3, 11.4Hz, 1H), 5.74(s, 1H), 4.96(dd, *J*=9.0, 3.6Hz, 1H), 3.94 (s, 3H), 3.46(dd, *J*=13.5, 3.6Hz, 1H), 3.17(s, 3H), 2.90(dd, *J*=13.5, 9.0Hz, 1H)
188	8.46(m, 2H), 7.51(m, 1H), 7.24(m, 1H), 7.14(d, *J*=11.1Hz, 1H), 7.02(m, 1H), 6.95(s, 1H), 6.88(d, *J*=8.1Hz, 1H), 6.73(d, *J*=15.3Hz, 1H), 6.59(dd, *J*=15.3, 11.1Hz, 1H), 5.81(s, 1H), 4.80(m, 1H), 3.94(s, 3H), 2.99(s, 3H), 2.69(m, 2H), 2.01(m, 1H), 1.82(m, 2H), 1.67(m, 1H)
189	8.47(d, *J*=3.3Hz, 1H), 7.46(d, *J*=7.8Hz, 1H), 7.20(m, 2H), 7.07(s, 2H), 6.70(d, *J*=15.3Hz, 1H), 6.50(dd, *J*=15.3, 11.1Hz, 1H), 4.02(m, 1H), 2.80 (m, 1H), 2.62(s, 3H), 2.59(m, 1H), 2.3(m, 1H), 2.34(s, 6H), 2.15(s, 6H)

Comp. No.	^{1}H NMR(300 MHz) δ
190	8.47(m, 1H), 7.46(m, 1H), 7.20(m, 2H), 7.07(s, 2H), 6.68(d, *J*=15.3Hz, 1H), 6.50(dd, *J*=15.3, 11.1Hz, 1H), 4.31(q, *J*=7.6Hz, 2H), 4.02(m, 1H), 2.80(m, 1H), 2.62(s, 3H), 2.59(m, 1H), 2.30(m, 1H), 2.34(s, 6H), 2.15(s, 6H), 1.25(t, *J*=7.6Hz, 3H)
193	8.64(m, 1H), 8.60(m, 1H), 7.77(m, 1H), 7.35(m, 1H), 7.24(d, *J*=11.1Hz, 1H), 7.08~7.00(m, 3H), 6.81(d, *J*=15.3Hz, 1H), 6.67(dd, *J*=15.3, 11.1Hz, 1H), 6.16(s, 1H), 4.31(q, *J*=7.2Hz, 2H), 3.94(m, 1H), 3.87(s, 3H), 2.82(m, 1H), 2.56(m, 1H), 2.31(m, 1H), 2.17(s, 6H), 1.38(t, *J*= 7.2Hz, 3H)
194	8.63~8.58(m, 2H), 7.66(m, 1H), 7.35(m, 1H), 7.24(s, 1H), 6.96(s, 2H), 6.65(s, 1H), 6.07(s, 1H), 3.95(m, 1H), 2.83(m, 1H), 2.55(m, 1H), 2.30(m, 1H), 2.24(s, 6H), 2.17(s, 6H), 2.15(s, 3H)
195	8.63(m, 2H), 7.69(m, 1H), 7.34(m, 1H), 7.19(s, 1H), 6.95(s, 2H), 6.61(s, 1H), 6.08(s, 1H), 3.95(m, 1H), 2.85(m, 1H), 2.60~2.30(m, 2H), 2.95(m, 1H), 2.24(s, 6H), 2.17(s, 6H), 1.18(t, *J*=7.6Hz, 3H)
196	8.63~8.58(m, 2H), 7.68(m, 1H), 7.35(m, 1H), 7.20(s, 1H), 6.93(s, 2H), 6.63(s, 1H), 6.07(s, 1H), 3.90(m, 1H), 2.85(m, 1H), 2.60~2.20(m, 4H), 2.24(s, 6H), 2.17(s, 6H), 1.69~1.22(m, 2H), 0.96(t, *J*=8.7Hz, 3H)
197	8.57~8.67(m, 2H), 7.62~7.73(m, 1H), 7.31~7.40(m, 1H), 7.26(d, *J*= 2.7Hz, 1H), 6.82~6.96(m, 2H), 6.73(s, 1H), 6.08(s, 1H), 5.29(s, 1H), 3.90~4.05(m, 1H), 3.89(s, 3H), 3.88(s, 3H), 2.77~2.93(m, 1H), 2.48~2.64(m, 1H), 2.27~2.40(m, 1H), 2.19(s, 6H), 2.22(d, *J*=0.9Hz, 3H)

Comp. No.	^{1}H NMR(300 MHz) δ
198	8.58~8.64(m, 2H), 7.65~7.68(m, 1H), 7.34~7.37(m, 1H), 7.24(d, *J*= 7.5Hz, 1H), 6.80~6.87(m, 4H), 6.69(s, 1H), 6.07(s, 1H), 3.98~4.01 (m, 1H), 3.88(s, 3H), 2.77~2.92(m, 1H), 2.48~2.64(m, 1H), 2.27~2.39 (m, 1H), 0.21(s, 3H), 2.19(s, 6H)
199	8.59(m, 2H), 7.62(m, 1H), 7.38(m, 1H), 7.20(s, 1H), 6.87(m, 2H), 6.85(s, 1H), 6.09(s, 1H), 5.29(s, 1H), 3.88(s, 3H), 3.85(m, 1H), 2.85(m, 1H), 2.52(m, 3H), 2.25(m; 1H), 2.17(s, 6H), 1.27(t, *J*=6.8Hz, 3H)
200	8.62(m, 2H), 7.64(m, 1H), 7.38(m, 1H), 7.19(s, 1H), 6.83(m, 3H), 6.66(s, 1H), 6.08(s, 1H), 3.98(m, 1H), 3.87(s, 3H), 2.85(m, 1H), 2.47(m, 4H), 2.19(s, 6H), 1.65(m, 2H), 0.94(t, *J*=6.8Hz, 3H)
207	8.60(m, 2H), 7.68(m, 1H), 7.35(m, 1H), 7.20(s, 1H), 6.65(s, 1H), 6.55 (s, 2H), 6.10(s, 1H), 3.95(m, 1H), 3.87(s, 6H), 2.85(m, 1H), 2.30~2.60 (m, 4H), 2.18(s, 6H), 1.21(t, *J*=7.6Hz, 3H)
208	8.62(m, 2H), 7.65(m, 1H), 7.38(m, 1H), 7.20(s, 1H), 6.65(s, 1H), 6.55(s, 2H), 6.10(s, 1H), 3.97(m, 1H), 3.88(s, 6H), 2.80(m, 1H), 2.54(m, 2H), 2.35(m, 2H), 2.19(s, 6H), 1.23(t, *J*=7.6Hz, 3H)
211	8.63(d, *J*=4.3Hz, 1H), 8.59(d, *J*=1.8Hz, 1H), 7.62~7.73(m, 1H), 7.36 dd, *J*=7.8, 4.8Hz, 1H), 7.13(d, *J*=7.8Hz, 1H), 7.06(s, 2H), 6.59(m, 3H), 6.21 (dd, *J*=13.8, 11.7Hz, 1H), 6.13(s, 1H), 3.98(m, 1H), 2.82(m, 1H), 2.59 (m, 1H), 2.38(m, 1H), 2.23(s, 6H), 2.17(s, 6H)

The present invention further relates to pharmaceutical compositions containing these compounds or acceptable salts thereof and the use of these compounds as antagonist of the PAF and/or inhibitor of the leukotriene. As stated above, compounds of the present invention possess activity of PAF-antagonist and/or

leukotriene-inhibition. Thus compounds of the invention may be used for the treatment and prophylaxis of diseases mediated or effected by PAF and leukotriene. The typical diseases for which the compounds of the present invention may be used as a therapeutic and prophylactic agent include inflammation (for example, arthritis, nephritis), circulatory diseases(for example, shock, thrombosis, transplant rejection, cerebral anemia, etc.) and allergic diseases (for example, asthma, psoriasis).

The compounds according to the invention, as well as the pharmaceutically acceptable salts thereof, have potent PAF-antagonistic and leukotriene-inhibitory activity. Accordingly the novel compounds may be used in pharmaceutical composition comprising a pharmaceutically effective amount of one of the compounds defined above and a pharmaceutically acceptable carrier. The inventive compounds are particularly useful as anti-allergic agents, anti-asthmatic agents, anti-psoriasis agents, anti-anaphylactic shock agents, anti-septic shock agents, anti-arthritic agents, anti-nephritic agents, anti-thromboplastic agents, anti-transplant rejection agents and anti-cerebral anemic agents.

The compounds accroding to the present invention, as well as the pharmaceutically acceptable salt thereof, may be incorporated into convenient dosage forms such as capsules, tablets, or injectable preparations. Solid or liquid pharmaceutically acceptable carriers may also be employed. Solid carriers include starch, lactose, calcium sulphate dihydrate, terra alba, sucrose, talc, gelatin, agar, pectin, acacia, magnesium stearate and stearic acid. Liquid carriers include syrup, peanut oil, olive oil, saline solution and water.

The carrier or diluent may include any prolonged release material, such as glyceryl monostearate or glyceryl distearate, alone or with wax. When a liquid carrier is used, the preparation may be in the form of a syrup, elixir, emulsion, soft gelatin capsule, sterile injectable liquid(e.g. solution) or a nonaqueous or aqueous liquid suspension.

The pharmaceutical preparations are prepared conventional techniques of the

pharmaceutical chemist.

Compounds according to the present invention may be administrated orally topically, parenterally, by inhalation spray or rectally in dosage unit formulations containing conventional non-toxic pharmaceutically acceptable carriers, adjuvants and vehicles.

The term parenteral as used herein includes subcutaneous injections, intravenous injection, intramuscular injection, intrasternal injection or infusion techniques.

An examplary daily dosage employed depends on the type of disease, the degree of symptom and age. The dosage levels of the compound in the above-indicated compositions may, of course, be varied and may conveniently be between about 0.01mg to about 200 mg per kilogram of the weight.

Pharmaceutical compositions containing compounds according to the invention may be in any form suitable for oral use, for example, as tablets, troches, lozenges, aqueous or oily suspensions, dispensable powders or granules, emulsion, hard or soft capsules, syrups or elixirs.

The tablets, capsules and the like may also contain a binder such as, e.g., lactose, saccharose, sorbitol, mannitol, starch, amylopectin, cellulose or gelatin; excipients such as, e.g., dicalcium phosphate; a disintegrating agent such as, e.g., corn starch or potato starch; a lubricant such as, e.g., magnesium stearate, calcium stearate, sodium stearylfumalate or polyethylene glycol wax. When the dosage unit form is a capsule, it may further contain, in addition to the types of materials described above, a liquid carrier such as e.g., a fatty oil.

These active compounds according to the present invention may also be administered parenterally. A solution or suspension of the active compounds may be prepared in water, optionally mixed with stabilizer or buffering agents. The dosages for parenteral administration are preferably as ampule or vial type.

These active compounds according to the invention may also be administered

by any known process of administrating the dose including topically, for example, an ointment, cream, jelly, solution, suspension or pachydematous patch; rectally, for example, suppository; intranasally or intrathoracally by inhalation spray.

Accordingly, the present invention provides pharmaceutical compositions comprising a pharmaceutically effective amount of thiazolidin-4-one derivatives and a pharmaceutically acceptable salt thereof. The present invention also provides the pharmaceutical uses of these compounds and compositions, especially for the prevent or treatment of various PAF- and/or leukotriene- induced diseases.

[pharmaceutical compositions]

Orally administration(Tablet) :

Composition	mg/Tablet	mg/Tablet
Active Ingredient	100	500
Lactose	122	113
Corn starch/water	30	40
Corn starch	45	40
Magnesium stearate	3	7
Total	300	700

Parenteral administration :

Composition	mg/vial	mg/vial
sterile active ingredient powder	100	500

※ Sterile water may be added to the above composition for intravenous injection.

The compounds of this invention were tested for pharmacological activity as described in the following pharmacology examples.

Pharmacology Example 1 : PAF-induced rabbit platelet aggregation.

Blood was collected from the ear artery of a male New Zealand white rabbit and mixed with 3.8 % sodium citrate in a 9:1 volume ratio. Platelet rich plasma(PRP) was obtained by centrifugation of blood at 150 g for 10 min at room temperature. The number of platelets was adjusted to 3 x 10^8 platelets/mL with platelet poor plasma. Platelet aggregation was monitored by continuous recording of light transmission in a dual-channel aggregometer(Chrono-Log 560-VS) coupled with a two channel recorder(Chrono-Log 707). Stirred PRP was treated with various concentration of test compounds or vehicle(0.5 % DMSO) for 2 min and then PAF(5 x 10^{-9} M) was added to induce platelet aggregation.

Inhibition values were calculated by comparing the extent of aggregation obtainted in the presence of the vehicle alone(0.5 % DMSO) and in the presence of a test compound. Log concentration-response curves were generated and the IC_{50} values were determined by regression analysis.

Pharmacology Example 2 : Inhibitory activity for LTB_4 biosynthesis

A suspension of rat basophillic leukemia-1 cell in phosphoric acid buffer solution with a concentration of 5×10^6/mL was allowed at 37℃ for 5 min and added the compound of thiazolidin-4-one. After allowed for 5 min, to the mixture was added arachidonic acid(25 μl/mL) and calcium ionophore A23187(1 μl/mL). After allowed for 15 min, the reaction mixture was quenched with 0.1N cooled hydrochloric acid and centrifuged with 3,300 rpm for 5 min. The supernatant solution was extracted with ethyl acetate and concentrated under nitrogen gas. The residue was dissolved in mobile phase and a amount of LTB_4 was determined with HPLC.

Table 7 lists result from this assay for inhibition of PAF-induced rabbit platelet aggregation and of LTB_4 biosynthesis for illustrative examples of the compounds of this invention.

Table 7 : Inhibitory activity of PAF-induced rabbit platelet aggregation and LTB_4 biosynthesis

Compound No.	PAF IC_{50} (μM)	Inhibition of LTB_4 biosynthesis (%, 10 μM)
1	1.741	30
2	0.058	47
3	0.079	54
4	0.211	67
6	1.901	85
7	0.065	74
8	1.348	45
9	15.21	63
10	0.535	92
11	0.496	89
12	0.141	42
13	0.329	37
14	4.21	75
15	2.101	47
16	3.21	25
17	0.721	43
18	0.071	62
19	0.046	65
20	3.37	43
21	1.021	89

Compound No.	PAF IC_{50} (μM)	Inhibition of LTB_4 biosynthesis (%, 10 μM)
22	0.274	41
23	0.058	57
38	2.123	92
39	7.21	99
40	0.501	42
63	0.258	39
64	0.526	47
67	3.21	100
68	1.37	100
69	1.21	65
70	4.74	75
71	2.53	67
72	4.21	17
73	5.22	100
74	4.72	100
78	3.73	45
79	6.73	100
80	7.21	65
81	25.7	25
82	4.21	30

Compound No.	PAF IC_{50} (μM)	Inhibition of LTB_4 biosynthesis (%, 10 μM)
83	12.7	36
84	25.8	100
85	12.1	35
86	15.7	40
87	25.1	50
88	30.2	48
89	22.7	100
90	4.21	42
91	13.72	65
92	12.71	38
93	12.71	43
94	27.2	17
95	11.7	49
96	10.5	37
97	13.5	27
98	12.8	42
99	12.5	52
100	13.7	100
101	14.2	42
102	12.6	37

Compound No.	PAF IC_{50} (μM)	Inhibition of LTB_4 biosynthesis (%, 10 μM)
103	13.8	100
104	14.7	48
105	12.7	47
106	21.6	38
107	9.76	63
108	12.1	63
109	13.6	57
110	12.7	37
111	12.4	100
112	11.3	67
115	12.5	28
116	13.7	98
117	13.4	42
118	15.4	98
119	9.78	45
120	7.21	100
121	8.47	72
122	8.52	100
123	27.2	52
124	25.7	100

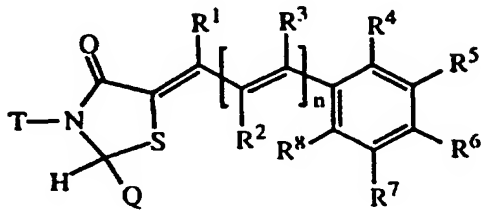
Compound No.	PAF IC_{50} (μM)	Inhibition of LTB_4 biosynthesis (%, 10 μM)
125	23.2	60
126	21.8	95
127	23.7	100
128	20.5	47
129	18.7	62
130	12.5	20
131	14.2	95
132	12.7	72
133	13.5	25
138	15.8	32
139	14.8	27
140	15.6	42
148	0.046	82
149	1.21	93
150	0.023	100
151	2.32	85
152	0.125	52
153	0.577	42
158	4.21	100
159	6.38	92

Compound No.	PAF IC_{50} (μM)	Inhibition of LTB_4 biosynthesis (%, 10 μM)
161	9.82	60
162	3.71	59
163	0.087	40
164	0.227	45
165	4.82	75
169	0.115	63
170	0.025	100
171	0.050	100
173	1.25	65
175	0.018	100
176	0.020	100
178	0.059	50
179	0.194	10
182	0.155	30
184	7.8	100
185	8.2	100
189	0.012	100
190	0.010	100
191	0.015	100
193	0.042	80

Compound No.	PAF IC_{50} (μM)	Inhibition of LTB_4 biosynthesis (%, 10 μM)
194	0.010	100
195	0.042	80
198	0.116	54
201	0.012	100
204	0.010	100
205	0.005	100
209	0.002	100
211	0.132	100
212	1.25	100

WHAT IS CLAIMED IS :

1. A compound of the following formula(I) or a pharmaceutically acceptable salt thereof



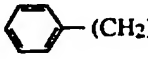
(I)

wherein,

n is 0, 1, 2 or 3;

Q is C_1 ~ C_{10} alkyl group, phenyl group that is optionally substituted with one or more suitable substituents selected from methoxy group and nitro group, or pyridiyl group that is optionally substituted with one or more methyl group;

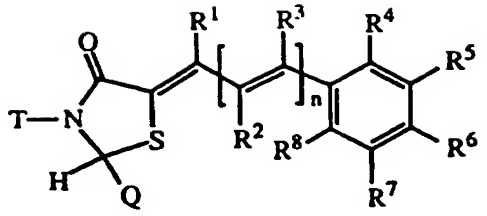
R^1, R^2 and R^3 are independently hydrogen atom, C_1 ~ C_{10} alkyl group, C_3 ~ C_6 cycloalkyl group or phenyl group that is optionally substituted with one or more methoxy group;

R^4, R^5, R^6, R^7 and R^8 are independently hydrogen atom, hydroxyl group, halogen atom, C_1 ~ C_{10} alkyl group, C_1 ~ C_{10} alkoxy group, nitro group, amino group that is optionally substituted with one or more suitable substituents selected from C_1 ~ C_{10} alkyl group and C_3 ~ C_6 cycloalkyl group, phenyl group that is optionally substituted with one or more suitable substituents selected from methoxy group and nitro group, C_1 ~ C_{10} haloalkyl group,  .

$-CO_2H$, $OCH_2OCH_2CH_2OCH_3$, $-OC(=O)-R^{15}$, $-OCO-R^{15}$, $-C(=O)-R^{15}$, $-C(=O)-NHR^{15}$, $-C(=O)-OR^{15}$, $-NHC(=O)-R^{15}$, $-CH_2NH-R^{15}$, $-N(OH)-C(=O)-NHR^{15}$, $-C(=O)-N(OH)R^{15}$, $-NHC(=O)-N(OH)R^{15}$, $-CH_2NHC(=O)-N(OH)-R^{15}$, $-OC(=O)-NR^{15}R^{15}$, $-OC(R^{16})_2-C(=O)-OR^{15}$, $-OCH_2-O-C(=O)-R^{15}$, $O-C(=O)-(CH_2)_m-C(=O)-OH$, or $-O-C(=O)-(CH_2)_m-C(=O)-OR^{15}$ (in which R^{15} is $C_1 \sim C_{10}$ alkyl group; and m is 1, 2, 3 or 4); and

T is hydrogen atom, hydroxyl group, $C_1 \sim C_{10}$ alkyl group, $-(CH_2)_m-R^9$, $-(CH_2)_m-O-R^{10}$, $-(CH_2)_m-C(=O)-R^{11}$, $-(CH_2)_m-NHC(=O)-R^{12}$, $-(CH_2)_m-N(OH)C(=O)-R^{16}$, $-(CH_2)_m-N(OH)C(=O)NH_2$, $-(CH_2)_m-C(=O)N(OH)-R^{16}$, or $-(CH_2)_m-NR^{13}R^{14}$ (in which, m is 1, 2, 3 or 4; R^9 is hydrogen atom, phenyl group that is optionally substituted with one or more suitable substituents selected from $C_1 \sim C_6$ alkyl group and $C_1 \sim C_6$ alkoxy group, or a pyridyl group; R^{10} is hydrogen atom, $C_1 \sim C_{10}$ alkyl group or $C_1 \sim C_4$ alkanoyl group; R^{11} is $C_1 \sim C_{10}$ alkyl group, $C_1 \sim C_{10}$ alkoxy group, or amino group that is optionally substituted with one or more suitable substituents selected from $C_1 \sim C_{10}$ alkyl group and $C_3 \sim C_6$ cycloalkyl group; R^{12} is $C_1 \sim C_{10}$ alkyl group or phenyl group; R^{13} is hydrogen atom, $C_1 \sim C_{10}$ alkyl group, or $C_1 \sim C_{10}$ alkanoyl group; R^{14} is hydrogen atom or $C_1 \sim C_{10}$ alkyl group or when taken together, connecting R^{13} and R^{14}, a substituted or unsubstituted four- to seven-membered cycloamino group, or a cycloamino group having another hetero atoms; and R^{16} is hydrogen atom or $C_1 \sim C_{10}$ alkyl group.

2. A pharmaceutical composition including a compound of the following formula (I) or a pharmaceutically acceptable salt thereof in combination with a pharmaceutically acceptable carrier



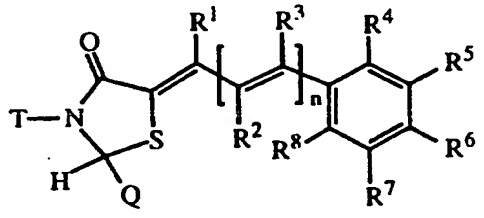
(I)

wherein, n, Q, T, R^1, R^2, R^3, R^4, R^5, R^6, R^7 and R^8 are respectively as definded in claim 1.

3. A process for treating PAF- and/or leukotriene-induced diseases which comprises the step of administering an effect amount of compound of formula (I) as claimed in claim 1 or pharmaceutically acceptable salt thereof, to a host in need of such treatement.

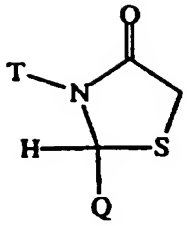
4. The process for treating PAF- and/or leukotriene-induced diseases as claimed in claim 3, the said diseases are arthritis, nephritis, anaphylactic shock, septic shock, thrombosis, transplant rejection, cerebral anemia, asthma or psoriasis.

5. A process for preparing compound of the following formula(I) or acceptable salt thereof



(I)

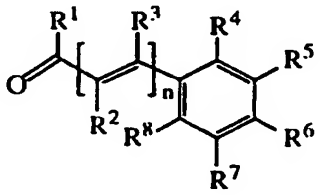
wherein, n, T, Q, R^1, R^2, R^3, R^4, R^5, R^6, R^7 and R^8 are respectively as definded in claim 1; reacting compound of the following formula(II)



(II)

wherein, T and Q are as in definded 1;

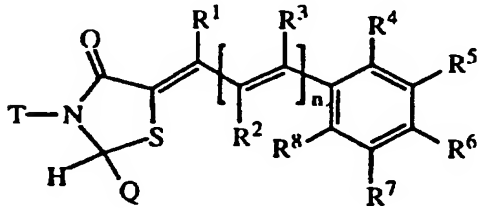
with compound of the following formula(III)



(III)

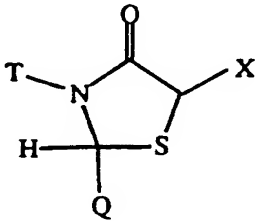
wherein, n, R^1, R^2, R^3, R^4, R^5, R^6, R^7 and R^8 are respectively as definded in claim 1.

6. A process for preparing compound of the following formula(I) or pharmaceutically acceptable salt thereof



(I)

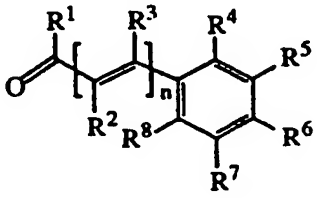
wherein, n, T, Q, R^1, R^2, R^3, R^4, R^5, R^6, R^7 and R^8 are respectively as definded in claim 1; reacting compound of the following formula(II-1)



(II-1)

wherein, T and Q are as definded in claim 1, and X is halogen atom;

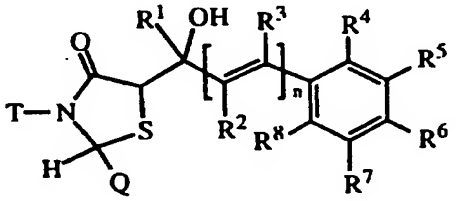
with compound of the following formula(III)



(III)

wherein, n, R^1, R^2, R^3, R^4, R^5, R^6, R^7 and R^8 are respectively as definded in claim 1;

to obtain compound of the following formula (I-1)

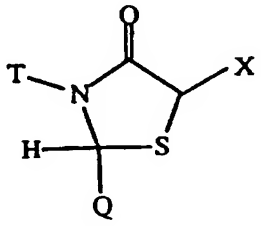


(I-1)

wherein, n, R^1, R^2, R^3, R^4, R^5, R^6, R^7 and R^8 are respectively as definded in claim 1; and

reacting the compound of the above formual(I-1) with an acid or alkali.

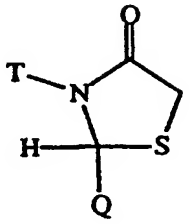
7. A process for preparing a compound having the following formual(II-1) by



(II-1)

wherein, T and Q are as definded in claim 1, and X is halogen atom;

reacting compound of the following formula(II)

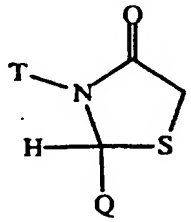


(II)

wherein, T and Q are as definded in claim 1;

with halides.

8. A process for preparing compound of the following formula(II) by



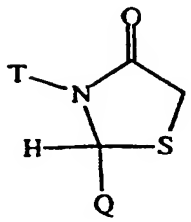
(II)

wherein, T and Q are definded as defined in claim 1;

dehydrating compound of Q-CHO(wherein, Q is as definded in claim 1) with compound of T-NH_2 (wherein, T is as definded in claim 1) and mercaptoacetic acid ($HSCH_2CO_2H$).

AMENDED CLAIMS

[received by the International Bureau on 3 May 1996 (03.05.96);
original claim 6 cancelled;
remainning claims unchanged (1 page)].



(II)

wherein, T and Q are as definded in claim 1;

with halides.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/KR 95/00183

A. CLASSIFICATION OF SUBJECT MATTER

IPC[6]: C 07 D 277/14,417/04,417/06,417/12,417/14; A 61 K 31/44

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC[6]: C 07 D 277/00, 417/00

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

AT, Chemical Abstracts

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Questel - DARC, CAS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 292 305 A1 (SUMITOMO) 23 November 1988 (23.11.88), example 63; page 2, lines 6-50; claim 1.	1-4
A	Chemical Abstracts, Vol.112, No.7, 12 February 1990 (Columbus, Ohio, USA), page 772, column 2, abstract No.55851q, ENOMOTO, M. et al.:"Optically active thiazolidin-4-ones as platelet activating factor (PAF) antagonists", Jpn. Kokai Tokkyo Koho JP 01,190,679.	1-4
A	Chemical Abstracts, Vol.96, No.21, 24 May 1982 (Columbus, Ohio, USA), page 704, column 1, abstract No.181185q, DASH, B. et al.:"Thiazolidone derivatives", J. Indian Chem. Soc. 1981, 58(12), 1184-6 (Eng).	1
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[X] Further documents are listed in the continuation of Box C. [X] See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
01 March 1996 (01.03.96)	15 March 1996 (15.03.96)

Name and mailing address of the ISA/ AT	Authorized officer
AUSTRIAN PATENT OFFICE Kohlmarkt 8-10 A-1014 Vienna	Hammer
Facsimile No. 1/53424/535	Telephone No. 1/5337058/44

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/KR 95/00183

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	Chemical Abstracts, Vol.92, No.13, 31 March 1980 (Columbus, Ohio, USA), page 653, column 2, abstract No.110910d, PANDYA, U.H. et al.:"Studies on thiazoli= dinones. Part VII", J. Inst. Chem. (India) 1979, 51(3), 129-30 (Eng).	8
Y	Chemical Abstracts, Vol.114, No.23, 10 June 1991 (Columbus, Ohio, USA), page 870, column 2, abstract No.229205r, DUNN, A.D. et al.:"Sulfur analogs of deoxyvasicinone. Part 5. Synthesis of methylated analogs", Z. Chem. 1990, 30(8), 288-9 (Eng).	8
Y	Chemical Abstracts, Vol.113, No.11, 10 September 1990 (Columbus, Ohio, USA), page 411, column 2, abstract No.94650p, PISCOPO, E. et al.:"Studies on heterocyclic compounds: 1,3-thiazolidin-4-one derivatives. IV. Biological activity of variously substituted 2,3-diaryl-1,3-thiazolidin-4-ones", Boll.-Soc. Ital. Biol. Sper. 1989, 65(9), 853-9 (Eng).	8
Y	EP 0 316 723 A1 (HOECHST-ROUSSEL) 24 May 1989 (24.05.89), example 5.	8
A	Chemical Abstracts, Vol.109, No.25, 19 December 1988 (Columbus, Ohio, USA), page 847, column 2, abstract No.230870g, SINGH, H. et al.:"Intramolecular chemo= selective heterocyclization of 4-oxothiazolidin-5-yl N-aryldithiocarbamates to fungitoxic 1,3-dithiolo-, 1,3-oxathiolo-, and thiazolothiazoles", Indian J. Chem. Sect. B 1987, 26B(12), 1200-2 (Eng).	7
A	Chemical Abstracts, Vol.112, No.9, 26 February 1990 (Columbus, Ohio, USA), page 785, column 1, abstract No.77014w, ZALESKA, B. et al.:"Substitution reactions of 2-(aroylmethylidene)thiazolidin-4-one derivatives", J. Prakt. Chem. 1989, 331(1), 55-60 (Eng).	7
A	Chemical Abstracts, Vol.84, No.25, 21 June 1976 (Columbus, Ohio, USA), page 566, column 2, abstract No.180117j, ASTIK, R.R. et al.:"Studies on thiazolidinones, Part 1", J. Indian Chem. Soc. 1975, 52(11), 1071-2 (Eng).	8
A	Chemical Abstracts, Vol.85, No.7, 16 August 1976 (Columbus, Ohio, USA), page 521, column 2, abstract No.46484u, ASTIK, R.R. et al.:"Studies on thiazolidionones, Part II", J. Indian Chem. Soc. 1976, 53(3), 272-3 (Eng).	8

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/KR 95/00183

In Recherchenbericht angeführtes Patentdokument Patent document cited in search report Document de brevet cité dans le rapport de recherche	Datum der Veröffentlichung Publication date Date de publication	Mitglied(er) der Patentfamilie Patent family member(s) Membre(s) de la famille de brevets	Datum der Veröffentlichung Publication date Date de publication
EP A1 292305	23-11-88	AT E 78821	15-08-92
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		DE T2 3873167	03-12-92
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		NO A 885[illegible]	22-05-89
		NO B 176143	31-10-94
		NO C 176143	08-02-95
		NZ A 226999	26-05-91
		PT A 89020	01-12-88
		PT B 89020	29-06-93
		ZA A 88[illegible]	27-09-89
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		US A 5[illegible]	06-12-94